Supplementary Information

Pd(II)-Catalyzed Cyclization of Alkyne-Tethered Malononitriles via Nitrile Insertion

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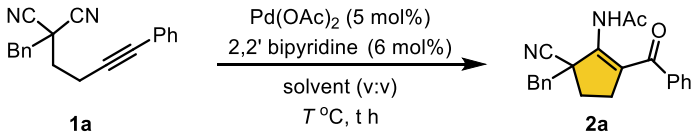
TABLE OF CONTENTS

I. General details

***General information*:** Unless otherwise noted, all reagents, solvents, catalysts and ligands were used as received from commercial suppliers. All palladium catalysts and ligands were purchased from Sigma-Aldrich and TCI. All reactions were performed under an inert atmosphere and in flame-dried or oven-dried glassware with magnetic stirring. Reactions were monitored using thin-layer chromatography (SiO_2). TLC plates were visualized with UV light (254 nm), iodine treatment, or using *p*-anisaldehyde stain or β-naphthol stain. Column chromatography was carried out using silica gel (100-200 mesh) packed in glass columns. NMR spectra were recorded at 300, 400, 500, 700 MHz (H) and at 75,100, 125, 176 MHz (C), respectively. Chemical shifts (δ) are reported in ppm, using the residual solvent peak in $CDCl_3$ (H: δ = 7.26 and C: δ = 77.16 ppm) as internal standard, and coupling constants (*J*) are given in Hz. HRMS were recorded using ESI-TOF techniques. Enantiomeric ratio (*er*) values were determined by chiral HPLC (Shimadzu LC-20AD) of the purified product and optical rotations of chiral compound was measured on polarimeter (Horiba SEPA-300).

II. Additional screening:

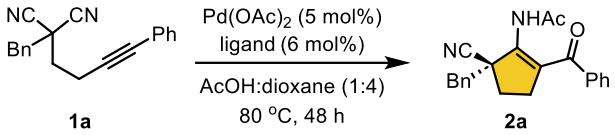
Table S1. Solvent screening[a]

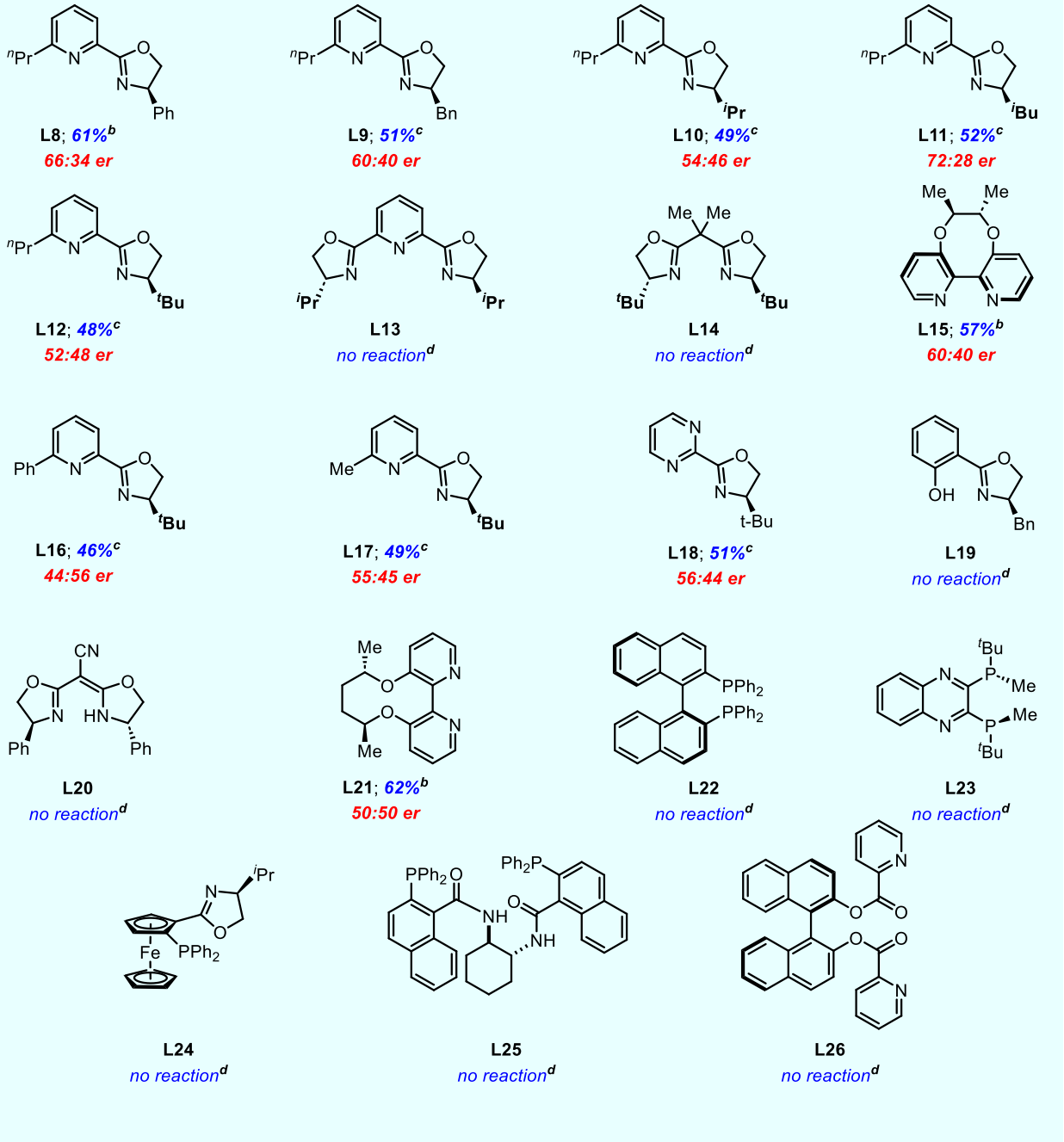


Entry	Solvent	Temperature (*T*)	Time (t)	Yield %
1	AcOH:DMF (1:4)	80 °C	36 h	21[b]
2	AcOH:THF (1:4)	65 °C	18 h	52[c]
3	AcOH:DCE (1:4)	65 °C	18 h	47[c]
4	AcOH:Toulene (1:4)	90 °C	12 h	59
5	AcOH:ACN (1:4)	70 °C	18 h	30[b]
6	AcOH:DCM (1:4)	50 °C	18 h	22[b]
7	AcOH:Et_2O (1:4)	45 °C	24 h	17[d]
8	AcOH:1,4 dioxane (1:4)	rt	24 h	NR[e]
9	AcOH:1,4 dioxane (1:4)	80 °C	12 h	81
10	AcOH:1,4 dioxane (1:9)	80 °C	12 h	76
11	AcOH (2 mL)	80 °C	12 h	68
12	1,4 dioxane (2 mL)	80 °C	12 h	NR[e]

[a] Reaction conditions: **1a** (0.2 mmol, 1 equiv), $Pd(OAc)_2$ (2.2 mg, 5 mol %), 2,2' bipyridine (1.9 mg, 6 mol %), in solvent (0.2 M), [b] more than 50% starting material was recovered, [c] more than 30% starting material was recovered, [d] more than 70% starting material was recovered, [e] more than 85% starting material was recovered, [NR] no reaction

Table S2. Ligands screening for asymmetric cyclization[a]

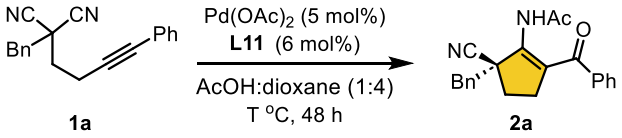




[a] Reaction conditions: **1a** (0.2 mmol, 1 equiv), $Pd(OAc)_2$ (2.2 mg, 5 mol %), ligand (6 mol %), AcOH in dioxane (1.0 mL, 0.2M); [b] more than 20% starting material was recovered; [c] 20-30% starting material was recovered; [d] more than 85% starting material was recovered.

Ligands **L8-L12**, **L16** and **L17** are prepared according to the reported procedure.[1] Ligands **L15** and **L21** are prepared by using the reported procedure.[2] Ligands **L19** and **L26** are prepared by using the reported procedure[3,4] and remaining all ligands are commercially available.

Table S3. Optimization of solvents with **L11** ligand



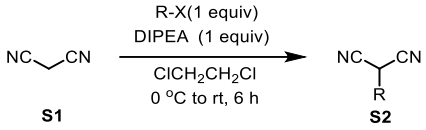
Entry	Solvent	Temperature	Yield %	er
1	DMF	80 °C	-[b]	-
2	THF	65 °C	45[c]	64:36
3	DCE	65 °C	-[b]	-
4	Toulene	80 °C	51[c]	70:30
5	ACN	80 °C	42[c]	49:51
6	CF_3Toulene	80 °C	44[c]	65:35
7	MeOH	80 °C	46[c]	63:37
8	1,4 dioxane	65 °C	50[d]	70:30
9	1,4 dioxane	80 °C	52[d]	72:28

[a] Reaction conditions: **1a** (0.2 mmol, 1 equiv), $Pd(OAc)_2$ (2.2 mg, 5 mol %), **L11** (2.9 mg, 6 mol %), AcOH in dioxane (1.0 mL, 0.2 M), [b] starting material was decomposed, [c] more than 30% starting material was recovered, [d] more than 20% starting material was recovered

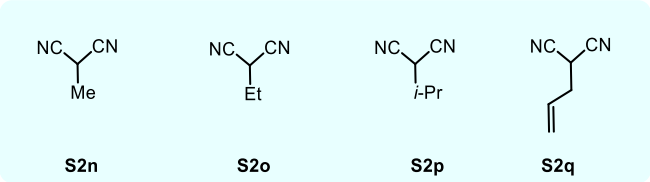
III. Experimental procedures and analytical data

IIIA. Experimental procedures and analytical data of substrates

a. General procedure for mono alkylation of malononitrile[5]

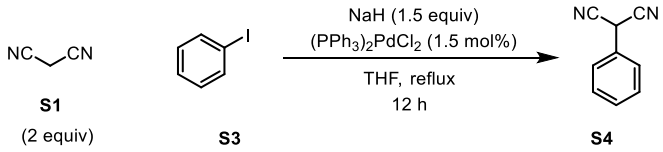


To a solution of malononitrile **S1** (15 mmol, 1 equiv) in dichloroethane (15 mL) under nitrogen atmosphere was cooled to 0 °C and added *N*,*N*-diisopropylethylamine (15 mmol, 1 equiv) and the appropriate alkyl halide (15 mmol, 1 equiv) dropwise, sequentially. The reaction mixture was left for stirring at room temperature for 6 hrs. After completion of the reaction (monitored by TLC), the reaction was quenched by adding 30 mL of water to the reaction mixture. After separating the organic layer, the aqueous layer was extracted with EtOAc (3 × 20 mL). The combined organic extract was washed with brine, dried over anhydrous sodium sulphate and the solvent was removed under reduced pressure. The crude concentrate was purified by flash column chromatography on silica gel (100-200 mesh) using EtOAc in hexanes as the eluent to afford the pure products (**S2**).



Substrates **S2n**, **S2o**, **S2p**, **S2q** were prepared by using the above procedure.

b. Procedure for the mono phenylation on malononitrile[6]

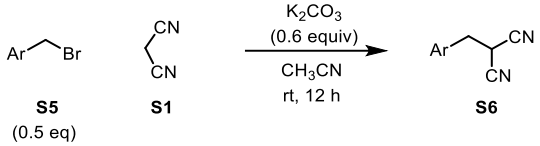


To a cooled (0 °C) slurry of NaH (480 mg, 12 mmol, 60 % in oil, pre-washed with dry hexane before use) in dry THF (20 mL) was added malononitrile **S1** (530 mg, 8 mmol) dropwise. Upon complete addition, the mixture was allowed to warm to ambient temperature. After the evolution of gas ceased, $Pd(PPh_3)_2Cl_2$ (255 mg, 0.36 mmol, 3 mol%) and iodobenzene **S3** (800 mg, 4 mmol) were added to the reaction mixture. The resulting mixture was stirred at reflux for overnight.

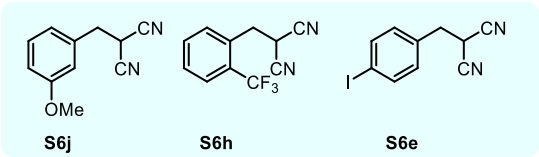
Afterwards, the mixture was cooled to room temperature, quenched carefully by the addition of water (10 mL), and concentrated *in vacuo*. Following extractive workup with EtOAc (2 x 20 mL), the combined organic layer was dried with sodium sulfate, filtered, and concentrated. The crude product was purified by chromatography on silica (10% EtOAc in hexanes; R_f = 0.5) to give phenyl malononitrile **S4** as a white solid (935 mg, 82% yield; mp = 66-68 ^oC).

c. General procedure for the mono benzylation on malononitrile

Procedure-A[7]

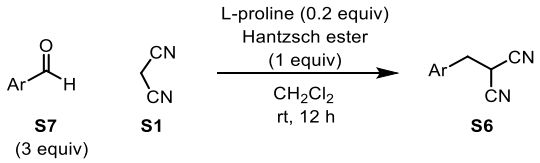


To a mixture of malononitrile **S1** (151 mmol), K_2CO_3 (91 mmol) in MeCN (50 mL) was added arylbromide **S5** (76 mmol), and the reaction mixture was stirred overnight under inert atmosphere. Later, H_2O (40 mL) and ethyl acetate (50 mL) were added to reaction mixture. The organic phase was separated and the aqueous phase was extracted with ethyl acetate (40 mL × 3). The combined organic phase was washed with H_2O (40 mL), brine, and dried over Na_2SO_4. The solvent was removed under vacuum and the residue was purified by column chromatography (hexane/ethyl acetate) to give monosubstituted malononitrile **S6**.



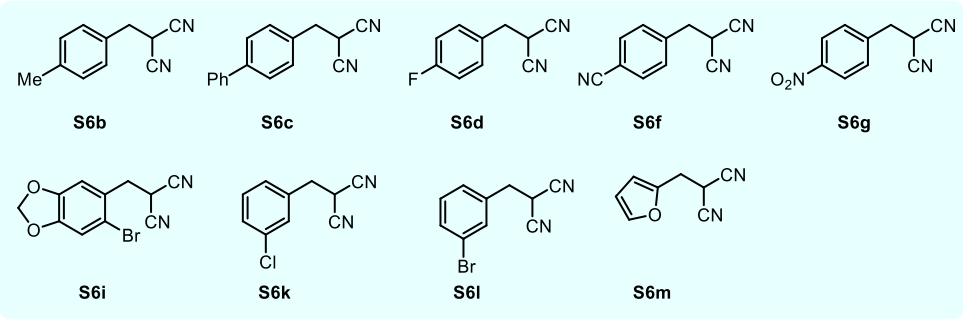
Substrates **S6j**, **S6h**, **S6e** are prepared by using procedure-A.

Procedure-B[8]



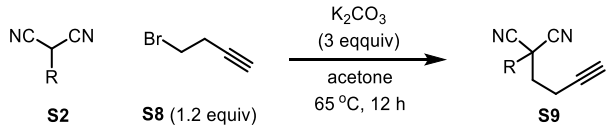
To a solution of aromatic aldehyde **S7** (454 mmol, 3.0 equiv) in CH_2Cl_2 (230 mL) were added malononitrile **S1** (151 mmol, 1.0 equiv), L-proline (30 mmol, 0.2 equiv), and Hantzsch ester (151 mmol, 1.0 equiv) sequentially at room temperature. The mixture was stirred at the room

temperature for 12 h. The solvent was removed under reduced pressure and the crude mixture was purified by flash column chromatography to give the desired product **S6**.



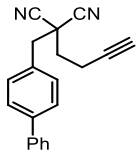
Substrates **S6b**, **S6c**, **S6d**, **S6f**, **S6g**, **S6i**, **S6k**, **S6k**, **S6l** & **S6m** are prepared by using procedure-B.

d. General procedure for the terminal alkyne-tethered malononitriles[8]



In an oven-dried pressure tube with a magnetic stirring bar were added 4-bromo-1-butyne (3.6 mmol, 1.2 equiv), monosubstituted malononitrile **S2** (3 mmol, 1.0 equiv), K_2CO_3 (9 mmol, 3.0 equiv), and 80 mL of acetone at room temperature. The flask was sealed and the mixture was stirred at the 65 ^oC for 12 h. Then the mixture was cooled to room temperature, filtered through a celite pad, and washed with EtOAc. The solvents were removed under reduced pressure to give a crude mixture. The crude mixture was purified by flash column chromatography to give the desired product alkyne-tethered malononitrile **S9**.

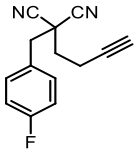
2-([1,1'-Biphenyl]-4-ylmethyl)-2-(but-3-yn-1-yl)malononitrile (S9c):



Prepared according to the general procedure as described above in 91% yield (775 mg). It was purified by flash chromatography (10% EtOAc/hexanes; R_f = 0.4) to afford a pale yellow solid; mp = 133-135 ^oC; ^1H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, *J* = 8.1 Hz, 2H), 7.61 (d, *J* = 7.4 Hz,

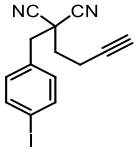
2H), 7.46 (t, *J* = 7.7 Hz, 4H), 7.38 (t, *J* = 7.3 Hz, 1H), 3.30 (s, 2H), 2.71 – 2.60 (m, 2H), 2.33 – 2.20 (m, 2H), 2.11 (t, *J* = 2.4 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.0, 140.3, 130.8, 130.5, 129.0, 127.9 (2C), 127.2, 114.7, 80.2, 71.1, 43.2, 38.7, 36.1, 15.7; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{20}H_{17}N_2^+$ 285.1392; Found 285.1410.

2-(But-3-yn-1-yl)-2-(4-fluorobenzyl)malononitrile (S9d):



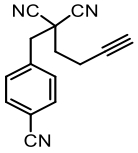
Prepared according to the general procedure as described above in 84% yield (570 mg). It was purified by flash chromatography (10% EtOAc/hexanes; R_f = 0.5) to afford a colorless solid; mp = 141-143 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 – 7.33 (m, 2H), 7.16 – 7.07 (m, 2H), 3.23 (s, 2H), 2.67 – 2.59 (m, 2H), 2.27 – 2.20 (m, 2H), 2.11 (t, *J* = 2.7 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.3 (d, *J* = 248.7 Hz), 132.1 (d, *J* = 8.4 Hz), 127.5 (d, *J* = 3.0 Hz), 116.3 (d, *J* = 21.7 Hz), 114.5, 80.1, 71.2, 42.8, 38.9, 36.1, 15.7; ^{19}F NMR (471 MHz, $CDCl_3$) δ -112.38 (s, 1F); IR (neat): υmax 3294, 2995, 2917, 2251, 1902, 1602, 1510, 1326, 1220, 1105, 827, 661 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{14}H_{12}FN_2^+$ 227.0985; Found 227.0977.

2-(But-3-yn-1-yl)-2-(4-iodobenzyl)malononitrile (S9e):



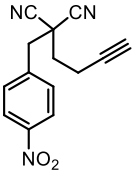
Prepared according to the general procedure as described above in 86% yield (862 mg). It was purified by flash chromatography (10% EtOAc/hexanes; R_f = 0.5) to afford a colorless solid; mp = 128-130 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.76 (dd, *J* = 8.6, 2.0 Hz, 2H), 7.17 – 7.09 (m, 2H), 3.19 (s, 2H), 2.70 – 2.57 (m, 2H), 2.29 – 2.18 (m, 2H), 2.10 (t, *J* = 2.7 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.4, 132.1, 114.4, 95.3, 80.0, 71.3, 43.0, 38.6, 36.2, 15.7; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{14}H_{12}IN_2^+$ 335.0045; Found 335.0029.

2-But-3-yn-1-yl)-2-(4-cyanobenzyl)malononitrile (S9f):



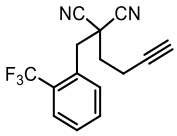
Prepared according to the general procedure as described above in 81% yield (566 mg). It was purified by flash chromatography (10% EtOAc/hexanes; R_f = 0.3) to afford a pale yellow solid; mp = 136-138 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 – 7.71 (m, 2H), 7.53 (d, *J* = 8.3 Hz, 2H), 3.31 (s, 2H), 2.69 – 2.61 (m, 2H), 2.30 – 2.24 (m, 2H), 2.12 (t, *J* = 2.7 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 136.8, 133.0, 131.2, 118.2, 114.1, 113.4, 79.8, 71.5, 43.2, 38.5, 36.4, 15.7; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{15}H_{12}N_3^+$ 234.1026; Found 234.1021.

2-(but-3-yn-1-yl)-2-(4-nitrobenzyl)malononitrile (S9g):



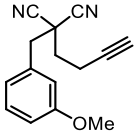
Prepared according to the general procedure as described above in 79% yield (600 mg). It was purified by flash chromatography (10% EtOAc/hexanes; R_f = 0.3) to afford a colorless solid; mp = 119-121 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 – 8.26 (m, 2H), 7.64 – 7.57 (m, 2H), 3.36 (s, 2H), 2.74 – 2.61 (m, 2H), 2.35 – 2.25 (m, 2H), 2.13 (t, *J* = 2.7 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.5, 138.7, 131.4, 124.4, 114.1, 79.8, 71.6, 42.9, 38.5, 36.4, 15.7; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{14}H_{12}O_2N_3^+$ 254.0929; Found 254.0916.

2-(But-3-yn-1-yl)-2-(2-(trifluoromethyl)benzyl)malononitrile (S9h):



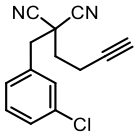
Prepared according to the general procedure as described above in 85% yield (704 mg). It was purified by flash chromatography (10% EtOAc/hexanes; R_f = 0.3) to afford a colorless solid; mp = 87-89 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 – 7.73 (m, 2H), 7.65 (t, *J* = 7.6 Hz, 1H), 7.52 (t, *J* = 7.7 Hz, 1H), 3.48 (s, 2H), 2.65 (ddd, *J* = 10.9, 6.5, 2.7 Hz, 2H), 2.37 – 2.27 (m, 2H), 2.11 (t, *J* = 2.7 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 132.7, 131.4, 130.9, 129.9 (q, J_{CF} = 29.7 Hz), 129.2, 127.2 (q, J_{CF} = 5.6 Hz), 124.1 (q, J_{CF} = 274.2 Hz), 114.6, 80.0, 71.2, 38.8, 38.1, 37.0, 15.7; ^{19}F NMR (471 MHz, $CDCl_3$) δ -57.16 (s, 3F); HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{15}H_{12}F_3N_2^+$ 277.0953; Found 277.0944.

2-(But-3-yn-1-yl)-2-(3-methoxybenzyl)malononitrile (S9j):



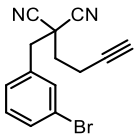
Prepared according to the general procedure as described above in 93% yield (664 mg). It was purified by flash chromatography (10% EtOAc/hexanes; R_f = 0.4) to afford a colorless solid; mp = 122-124 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32 (td, *J* = 7.7, 0.8 Hz, 1H), 6.98 – 6.90 (m, 3H), 3.83 (s, 3H), 3.23 (s, 2H), 2.62 (ddd, *J* = 10.9, 6.4, 2.7 Hz, 2H), 2.27 – 2.16 (m, 2H), 2.09 (t, *J* = 2.7 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.0, 133.0, 130.2, 122.6, 115.9, 114.7, 114.6, 80.2, 71.1, 55.4, 43.5, 38.5, 36.1, 15.7; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{15}H_{15}N_2O^+$ 239.1184; Found 239.1175.

2-(But-3-yn-1-yl)-2-(3-chlorobenzyl)malononitrile (S9k):



Prepared according to the general procedure as described above in 90% yield (653 mg). It was purified by flash chromatography (10% EtOAc/hexanes; R_f = 0.5) to afford a colorless solid; mp = 137-139 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 – 7.33 (m, 3H), 7.31 – 7.27 (m, 1H), 3.23 (s, 2H), 2.63 (ddd, *J* = 8.3, 7.0, 2.7 Hz, 2H), 2.27 – 2.20 (m, 2H), 2.11 (t, *J* = 2.7 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 135.1, 133.5, 130.5, 130.4, 129.4, 128.5, 114.4, 80.0, 71.3, 43.0, 38.5, 36.2, 15.7; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{14}H_{12}ClN_2^+$ 243.0689; Found 243.0676.

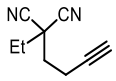
2-(3-Bromobenzyl)-2-(but-3-yn-1-yl)malononitrile (S9l):



Prepared according to the general procedure as described above in 83% yield (715 mg). It was purified by flash chromatography (10% EtOAc/hexanes; R_f = 0.5) to afford a colorless solid; mp = 110-112 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 – 7.51 (m, 2H), 7.36 – 7.27 (m, 2H), 3.22 (s, 2H), 2.74 – 2.55 (m, 2H), 2.31 – 2.18 (m, 2H), 2.11 (t, *J* = 2.7 Hz, 1H); ^{13}C NMR (101 MHz,

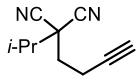
$CDCl_3$) δ 133.8, 133.3, 132.4, 130.7, 129.0, 123.1, 114.4, 80.0, 71.3, 42.9, 38.5, 36.1, 15.7; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{14}H_{12}BrN_2^+$ 287.0178; Found 287.0169.

2-(But-3-yn-1-yl)-2-ethylmalononitrile (S9o):



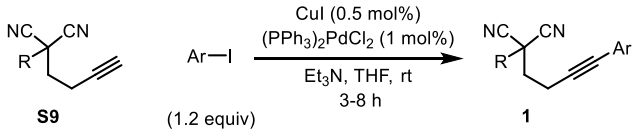
Prepared according to the general procedure as described above in 87% yield (381 mg). It was purified by flash chromatography (10% EtOAc/hexanes; R_f = 0.3) to afford a colorless oil; ^1H NMR (400 MHz, $CDCl_3$) δ 2.63 – 2.54 (m, 2H), 2.24 – 2.16 (m, 2H), 2.09 (t, *J* = 2.7 Hz, 1H), 2.03 (q, *J* = 7.4 Hz, 2H), 1.29 (td, *J* = 7.4, 0.6 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 114.8, 80.2, 70.9, 38.0, 35.9, 31.6, 15.5, 9.9; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_9H_{11}N_2^+$ 147.0922; Found 147.0913.

2-(But-3-yn-1-yl)-2-isopropylmalononitrile (S9p):



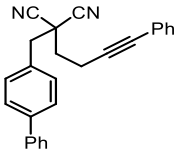
Prepared according to the general procedure as described above in 81% yield (389 mg). It was purified by flash chromatography (10% EtOAc/hexanes; R_f = 0.3) to afford a colorless oil; ^1H NMR (400 MHz, $CDCl_3$) δ 2.64 – 2.55 (m, 2H), 2.26 – 2.14 (m, 3H), 2.09 (t, *J* = 2.7 Hz, 1H), 1.25 (d, *J* = 6.7 Hz, 6H); ^{13}C NMR (176 MHz, $CDCl_3$) δ 114.4, 80.3, 70.9, 43.2, 35.7, 34.1, 18.4, 15.7; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{10}H_{13}N_2^+$ 161.1078; Found 161.1068.

e. General procedure for the sonagashira coupling[9]



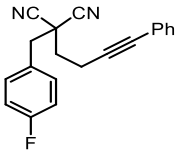
To a solution of alkyne-tethered malononitrile, **S9** (2 mmol) in degassed Et_3N (0.08 M, 1 mL), THF (4 mL) was added $Pd(PPh_3)_2Cl_2$ (0.02 mmol, 1 mol%), CuI (0.01 mmol, 0.5 mol%) and aryl iodide (2.4 mmol). The mixture was stirred at room temperature for 3-8 hours. The reaction was cooled to room temperature, Water (10 mL) was added, and the mixture was extracted with EtOAc (3 × 8 mL). The combined organic solvent was washed with 10% aqueous HCl (4 mL), dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The mixture was purified by column chromatography (EtOAc/hexane) to give aryl-substituted alkynes **1** in high yields.

2-([1,1'-Biphenyl]-4-ylmethyl)-2-(4-phenylbut-3-yn-1-yl)malononitrile (1c):



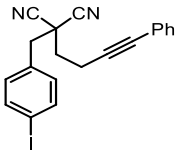
Prepared according to the general procedure as described above in 88% yield (634 mg). It was purified by flash chromatography (10% EtOAc/hexanes; R_f = 0.4) to afford a colorless solid; mp = 143-145 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ 7.65 (d, *J* = 8.1 Hz, 2H), 7.61 (d, *J* = 7.8 Hz, 2H), 7.49 – 7.45 (m, 4H), 7.45 – 7.41 (m, 2H), 7.38 (t, *J* = 7.3 Hz, 1H), 7.35 – 7.28 (m, 3H), 3.34 (s, 2H), 2.88 (dd, *J* = 7.6, 8.1 Hz, 2H), 2.33 (dd, *J* = 8.1, 7.5 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.0, 140.3, 131.7, 130.9, 130.6, 129.0, 128.4, 128.4, 127.9, 127.8, 127.2, 123.0, 114.9, 85.5, 83.1, 43.3, 38.7, 36.2, 16.7; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{26}H_{21}N_2^+$ 361.1699; Found 361.1685.

2-(4-Fluorobenzyl)-2-(4-phenylbut-3-yn-1-yl)malononitrile (1d):



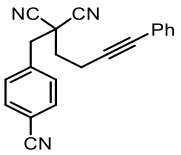
Prepared according to the general procedure as described above in 68% yield (411 mg). It was purified by flash chromatography (10% EtOAc/hexanes; R_f = 0.5) to afford a pale yellowish solid; mp = 138-140 ^oC; ^1H NMR (400 MHz, $CDCl_3$) δ 7.45 – 7.36 (m, 4H), 7.35 – 7.27 (m, 3H), 7.16 – 7.08 (m, 2H), 3.27 (s, 2H), 2.86 (dd, *J* = 7.5, 8.1 Hz, 2H), 2.30 (dd, *J* = 8.0, 7.5 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.2 (d, *J* = 248.5 Hz), 132.2 (d, *J* = 8.4 Hz), 131.7, 128.4, 128.4, 127.6 (d, *J* = 2.8 Hz), 122.9, 116.2 (d, *J* = 21.7 Hz), 114.7, 85.4, 83.1, 42.9, 38.9, 36.3, 16.7; ^{19}F NMR (377 MHz, $CDCl_3$) δ -112.44 (s, 1F); HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{20}H_{16}FN_2^+$ 303.1292; Found 303.1281.

2-(4-Iodobenzyl)-2-(4-phenylbut-3-yn-1-yl)malononitrile (1e):



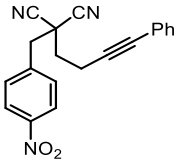
Prepared according to the general procedure as described above in 83% yield (681 mg). It was purified by flash chromatography (10% EtOAc/hexanes; R_f = 0.5) to afford a brownish solid; mp = 146-148 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.1 Hz, 2H), 7.45 – 7.38 (m, 2H), 7.30 (d, *J* = 4.9 Hz, 3H), 7.15 (d, *J* = 8.0 Hz, 2H), 3.23 (s, 2H), 2.86 (t, *J* = 7.7 Hz, 2H), 2.29 (t, *J* = 7.7 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.4, 132.2, 131.7, 131.3, 128.5, 128.4, 122.9, 114.6, 95.2, 85.3, 83.2, 43.1, 38.6, 36.3, 16.7; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{20}H_{16}IN_2^+$ 411.0353; Found 411.0333.

2-(4-Cyanobenzyl)-2-(4-phenylbut-3-yn-1-yl)malononitrile (1f):



Prepared according to the general procedure as described above in 69% yield (426 mg). It was purified by flash chromatography (10% EtOAc/hexanes; R_f = 0.3) to afford a colorless solid; mp = 135-137 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 8.1 Hz, 2H), 7.54 (d, *J* = 8.0 Hz, 2H), 7.44 – 7.38 (m, 2H), 7.31 (d, *J* = 5.0 Hz, 3H), 3.34 (s, 2H), 2.88 (t, *J* = 7.6 Hz, 2H), 2.34 (t, *J* = 7.7 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 136.9, 132.9, 131.7, 131.2, 128.5, 122.8, 118.2, 114.3, 113.4, 85.1, 83.4, 43.4, 38.5, 36.5, 16.7; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{21}H_{16}N_3^+$ 310.1339; Found 310.1328.

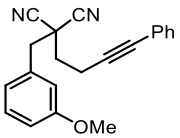
2-(4-Nitrobenzyl)-2-(4-phenylbut-3-yn-1-yl)malononitrile (1g):



Prepared according to the general procedure as described above in 67% yield (441 mg). It was purified by flash chromatography (10% EtOAc/hexanes; R_f = 0.3) to afford a yellowish brown solid; mp = 124-126 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (d, *J* = 8.6 Hz, 2H), 7.61 (d, *J* = 8.5 Hz, 2H), 7.45 – 7.38 (m, 2H), 7.30 (dd, *J* = 7.0, 3.2 Hz, 3H), 3.40 (s, 2H), 2.89 (t, *J* = 7.6 Hz, 2H), 2.36 (t, *J* = 7.7 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.5, 138.8, 131.7, 131.5, 128.5, 124.4,

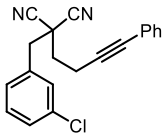
122.8, 114.2, 85.0, 83.5, 43.0, 38.5, 36.6, 16.7; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{20}H_{16}O_2N_3^+$ 330.1237; Found 330.1225.

2-(3-Methoxybenzyl)-2-(4-phenylbut-3-yn-1-yl)malononitrile (1j):



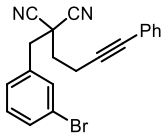
Prepared according to the general procedure as described above in 72% yield (452 mg). It was purified by flash chromatography (10% EtOAc/hexanes; R_f = 0.4) to afford a yellowish brown solid; mp = 103-105 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (dd, *J* = 6.6, 3.0 Hz, 2H), 7.37 – 7.28 (m, 4H), 7.00 – 6.92 (m, 3H), 3.83 (s, 3H), 3.26 (s, 2H), 2.86 (dd, *J* = 7.5, 8.1 Hz, 2H), 2.29 (dd, *J* = 8.1, 7.6 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.0, 133.1, 131.7, 130.2, 128.4, 128.4, 128.4, 123.0, 122.6, 115.9, 114.9, 114.6, 85.5, 83.0, 55.4, 43.6, 38.6, 36.2, 16.6; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{21}H_{19}ON_2^+$ 315.1492; Found 315.1481.

2-(3-Chlorobenzyl)-2-(4-phenylbut-3-yn-1-yl)malononitrile (1k):



Prepared according to the general procedure as described above in 84% yield (534 mg). It was purified by flash chromatography (10% EtOAc/hexanes; R_f = 0.5) to afford a brownish solid; mp = 123-125 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 – 7.38 (m, 4H), 7.38 – 7.34 (m, 1H), 7.34 – 7.27 (m, 4H), 3.26 (s, 2H), 2.87 (dd, *J* = 7.5, 8.0 Hz, 2H), 2.31 (dd, *J* = 8.0, 7.5 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 135.1, 133.6, 131.7, 130.5, 129.4, 128.6, 128.5, 128.4, 122.9, 114.5, 85.3, 83.2, 43.1, 38.5, 36.3, 16.7; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{20}H_{16}ClN_2^+$ 319.0996; Found 319.0986.

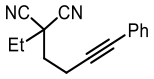
2-(3-Bromobenzyl)-2-(4-phenylbut-3-yn-1-yl)malononitrile (1l):



Prepared according to the general procedure as described above in 79% yield (573 mg). It was purified by flash chromatography (10% EtOAc/hexanes; R_f = 0.5) to afford a brownish solid; mp = 106-108 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.57 – 7.54 (m, 2H), 7.45 – 7.40 (m, 2H), 7.37 –

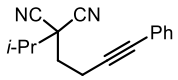
7.35 (m, 1H), 7.30 (ddd, *J* = 6.0, 4.4, 2.6 Hz, 4H), 3.25 (s, 2H), 2.87 (dd, *J* = 7.5, 8.0 Hz, 2H), 2.30 (dd, *J* = 7.9, 7.6 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 133.9, 133.3, 132.3, 131.7, 130.7, 129.0, 128.5, 128.4, 123.1, 122.9, 114.5, 85.3, 83.2, 43.0, 38.5, 36.3, 16.7; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{20}H_{16}BrN_2^+$ 363.0491; Found 363.0474.

2-Ethyl-2-(4-phenylbut-3-yn-1-yl)malononitrile (1o):



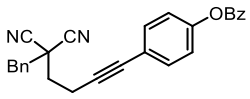
Prepared according to the general procedure as described above in 77% yield (342 mg). It was purified by flash chromatography (10% EtOAc/hexanes; R_f = 0.3) to afford a yellowish semi solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 – 7.39 (m, 2H), 7.33 – 7.28 (m, 3H), 2.82 (dd, *J* = 7.5, 8.1 Hz, 2H), 2.27 (dd, *J* = 8.0, 7.6 Hz, 2H), 2.08 (q, *J* = 7.4 Hz, 2H), 1.32 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 131.7, 128.4, 128.3, 123.0, 115.1, 85.6, 82.9, 38.1, 36.2, 31.8, 16.5, 10.0; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{15}H_{15}N_2^+$ 223.1235; Found 223.1233.

2-Isopropyl-2-(4-phenylbut-3-yn-1-yl)malononitrile (1p):



Prepared according to the general procedure as described above in 81% yield (382 mg). It was purified by flash chromatography (10% EtOAc/hexanes; R_f = 0.3) to afford a colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (ddd, *J* = 5.3, 4.6, 2.7 Hz, 2H), 7.33 – 7.27 (m, 3H), 2.83 (dd, *J* = 8.7, 7.2 Hz, 2H), 2.31 – 2.22 (m, 3H), 1.28 (d, *J* = 6.7 Hz, 6H); ^{13}C NMR (176 MHz, $CDCl_3$) δ 131.7, 128.4, 128.3, 123.0, 114.6, 85.7, 82.8, 43.2, 35.9, 34.4, 18.5, 16.8; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{16}H_{17}N_2^+$ 237.1386; Found 237.1384.

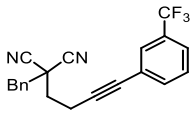
4-(5,5-Dicyano-6-phenylhex-1-yn-1-yl)phenyl benzoate (1y):



Prepared according to the general procedure as described above in 74% yield (485 mg). It was purified by flash chromatography (10% EtOAc/hexanes; R_f = 0.4) to afford a colorless solid; mp = 167-169 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (dt, *J* = 8.5, 1.5 Hz, 2H), 7.65 (tt, *J* = 7.4, 1.3

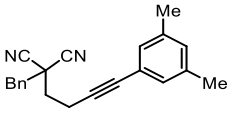
Hz, 1H), 7.55 – 7.46 (m, 4H), 7.45 – 7.37 (m, 5H), 7.17 (dt, *J* = 8.7, 2.0 Hz, 2H), 3.30 (s, 2H), 2.87 (dd, *J* = 7.5, 8.1 Hz, 2H), 2.30 (dd, *J* = 8.0, 7.6 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.0, 150.9, 133.9, 133.0, 131.7, 130.4, 130.3, 129.4, 129.2, 129.1, 128.8, 122.0, 120.7, 114.8, 85.7, 82.3, 43.7, 38.7, 36.2, 16.7; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{27}H_{21}O_2N_2^+$ 405.1597; Found 405.1589.

2-Benzyl-2-(4-(3-(trifluoromethyl)phenyl)but-3-yn-1-yl)malononitrile (1z):



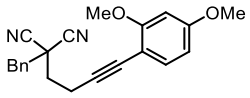
Prepared according to the general procedure as described above in 76% yield (535 mg). It was purified by flash chromatography (10% EtOAc/hexanes; R_f = 0.3) to afford a colorless solid; mp = 99-101 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (s, 1H), 7.57 (dd, *J* = 12.0, 7.8 Hz, 2H), 7.46 – 7.38 (m, 6H), 3.29 (s, 2H), 2.87 (dd, *J* = 7.5, 8.0 Hz, 2H), 2.30 (dd, *J* = 8.4, 7.2 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 134.9, 131.6, 131.0 (q, J_{CF} = 32.5 Hz), 128.5 (q, J_{CF} = 3.6 Hz), 130.4, 129.2, 129.1, 129.0, 125.0 (q, J_{CF} = 3.4 Hz), 123.9, 123.8 (q, J_{CF} = 272.4 Hz), 114.8, 87.2, 81.7, 43.8, 38.7, 36.1, 16.6; ^{19}F NMR (377 MHz, $CDCl_3$) δ -63.00 (s, 3F); HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{21}H_{16}F_3N_2^+$ 353.1266; Found 353.1251.

2-Benzyl-2-(4-(3,5-dimethylphenyl)but-3-yn-1-yl)malononitrile (1aa):



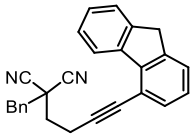
Prepared according to the general procedure as described above in 81% yield (505 mg). It was purified by flash chromatography (10% EtOAc/hexanes; R_f = 0.4) to afford a colorless solid; mp = 133-135 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.39 (m, 5H), 7.05 (s, 2H), 6.95 (s, 1H), 3.29 (s, 2H), 2.84 (dd, *J* = 7.6, 8.1 Hz, 2H), 2.31 – 2.26 (m, 8H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 138.0, 131.8, 130.4, 130.3, 129.4, 129.2, 129.1, 122.6, 114.8, 84.7, 83.3, 43.6, 38.7, 36.3, 21.2, 16.7; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{22}H_{21}N_2^+$ 313.1699; Found 313.1697.

2-Benzyl-2-(4-(2,4-dimethoxyphenyl)but-3-yn-1-yl)malononitrile (1ab):

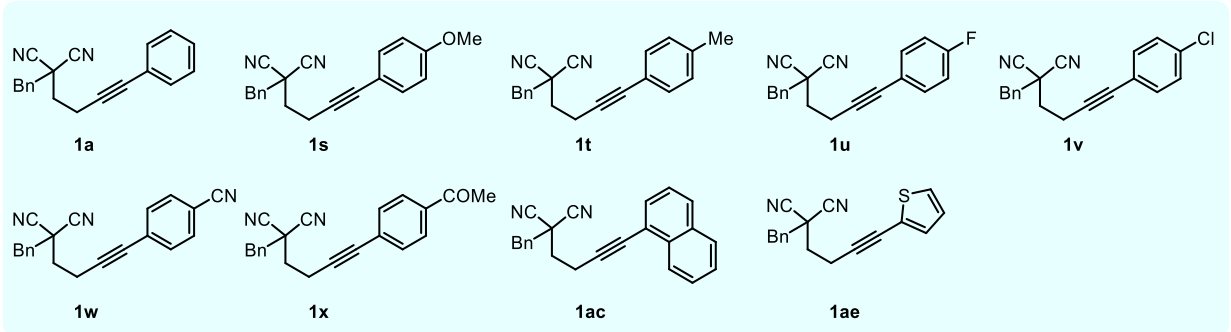


Prepared according to the general procedure as described above in 82% yield (564 mg). It was purified by flash chromatography (10% EtOAc/hexanes; R_f = 0.4) to afford a pale yellowish semisolid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 – 7.37 (m, 5H), 7.36 – 7.28 (m, 1H), 6.47 – 6.40 (m, 2H), 3.83 (s, 3H), 3.81 (s, 3H), 3.31 (s, 2H), 2.90 (dd, *J* = 8.5, 7.2 Hz, 2H), 2.32 (dd, *J* = 8.5, 7.2 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.3, 161.2, 134.5, 131.9, 130.4, 129.1, 129.0, 114.9, 104.9, 104.6, 98.5, 88.1, 79.1, 55.9, 55.6, 43.4, 38.8, 36.4, 17.0; IR (neat): υmax 2937, 2857, 2840, 2247, 1606, 1572, 1505, 1417, 1209, 703 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{22}H_{21}O_2N_2^+$ 345.1597; Found 345.1595.

2-(4-(9*H*-Fluoren-1-yl)but-3-yn-1-yl)-2-benzylmalononitrile (1ad):

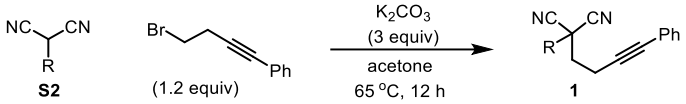


Prepared according to the general procedure as described above in 79% yield (588 mg). It was purified by flash chromatography (10% EtOAc/hexanes; R_f = 0.4) to afford a colorless solid; mp = 157-159 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 7.5 Hz, 1H), 7.71 (d, *J* = 7.9 Hz, 1H), 7.60 (s, 1H), 7.55 (d, *J* = 7.4 Hz, 1H), 7.46 – 7.36 (m, 7H), 7.32 (td, *J* = 7.4, 1.1 Hz, 1H), 3.88 (s, 2H), 3.30 (s, 2H), 2.89 (dd, *J* = 7.5, 8.1 Hz, 2H), 2.31 (dd, *J* = 8.1, 7.6 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.6, 143.3, 142.0, 141.1, 131.8, 130.6, 130.4, 129.2, 129.1, 128.3, 127.3, 127.0, 125.20, 121.0, 120.3, 119.9, 114.9, 85.4, 83.7, 43.6, 38.7, 36.8, 36.3, 16.8; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{27}H_{21}N_2^+$ 373.1699; Found 373.1694.

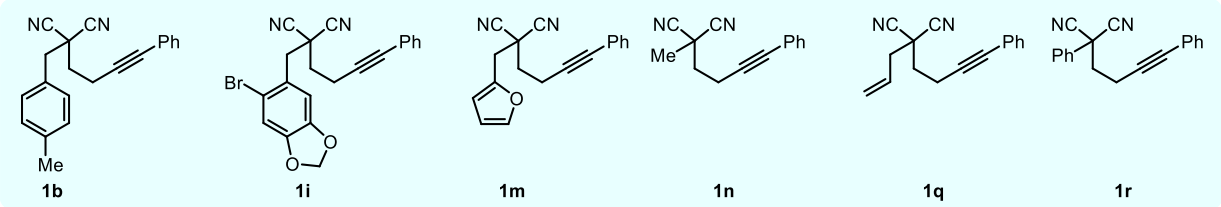


Substrates **1a**, **1s**, **1t**, **1u**, **1v**, **1w**, **1x**, **1ac**, and **1ae** were synthesized through a previous literature report.[8]

f. General procedure for the internal alkyne-tethered malononitriles[8]



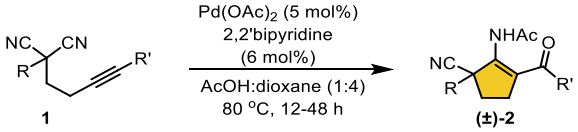
In an oven-dried pressure tube with a magnetic stirring bar were added (4-bromobut-1-yn-1-yl)benzene (3.6 mmol, 1.2 equiv), monosubstituted malononitrile **S2** (3 mmol, 1.0 equiv), K_2CO_3 (9 mmol, 3.0 equiv), and 80 mL of acetone at room temperature. The flask was sealed and the mixture was stirred at the 65 ^oC for 12 h. Then the mixture was cooled to room temperature, filtered through a celite pad, and washed with EA (13 mL x 3). The solvents were removed under reduced pressure to give a crude mixture. The crude mixture was purified by flash column chromatography to give the desired product alkyne-tethered malononitrile **1**.



Substrates **1b**, **1i**, **1m**, **1n**, **1q**, **1r** are prepared by using the above procedure.

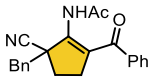
IIIB. Experimental procedures and analytical data of the products

a. General procedure for tandem cyclization of alkyne-tethered malononitriles



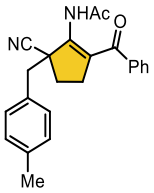
A dried screw-cap vial was charged with alkyne-tethered malononitrile **1** (0.2 mmol), $Pd(OAc)_2$ (5 mol%, 0.01 mmol), and 2,2′bipyridine (6 mol%, 0.012 mmol) in AcOH:1,4 dioxane (1:4 ratio, 0.2+0.8 mL) under N_2 atmosphere at rt. The reaction mixture was stirred at 80 ^oC in preheated oil bath for 12-48 hours (monitored by TLC). After the completion of the reaction, it was cooled to room temperature and quenched with aqueous $NaHCO_3$ (8 mL) solution. The mixture was extracted with EtOAc (3x8 mL) and concentrated under reduced pressure. The residue was directly subjected to flash column chromatography on silica gel (hexanes/ethyl acetate) to afford the desired product **2**.

***N*-(2-Benzoyl-5-benzyl-5-cyanocyclopent-1-en-1-yl)acetamide (2a):**



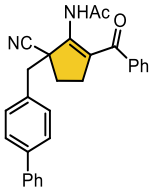
Prepared according to the general procedure as described above in 12 h with 81% yield (56 mg). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.4) to afford a brown solid; mp = 151-153 ^oC; ^1H NMR (400 MHz, $CDCl_3$) δ 11.66 (s, 1H), 7.53 – 7.48 (m, 1H), 7.46 – 7.38 (m, 4H), 7.36 – 7.31 (m, 5H), 3.62 (d, *J* = 13.3 Hz, 1H), 3.24 (d, *J* = 13.3 Hz, 1H), 2.54 – 2.48 (m, 1H), 2.42 (ddd, *J* = 16.8, 12.7, 8.1 Hz, 2H), 2.37 – 2.31 (m, 1H), 2.30 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.3, 168.0, 151.6, 139.4, 135.1, 132.1, 130.5, 128.6, 128.5, 127.7, 127.6, 121.0, 118.4, 48.8, 40.6, 36.3, 29.5, 24.9; IR (neat): υmax 3284, 2924, 2857, 2237, 1713, 1624, 1574, 1449, 1263, 704 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{22}H_{21}N_2O_2^+$ 345.1597; Found 345.1596.

***N*-(2-benzoyl-5-cyano-5-(4-methylbenzyl)cyclopent-1-en-1-yl)acetamide (2b):**



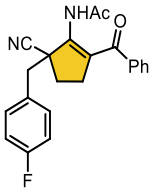
Prepared according to the general procedure as described above in 12 h with 80% yield (57 mg). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.4) to afford a reddish brown semi-solid; ^1H NMR (400 MHz, $CDCl_3$) δ 11.63 (s, 1H), 7.53 – 7.48 (m, 1H), 7.45 (dd, *J* = 9.9, 3.1 Hz, 2H), 7.43 – 7.38 (m, 2H), 7.23 (d, *J* = 8.0 Hz, 2H), 7.15 (d, *J* = 7.8 Hz, 2H), 3.58 (d, *J* = 13.3 Hz, 1H), 3.20 (d, *J* = 13.4 Hz, 1H), 2.51 (ddd, *J* = 13.9, 8.9, 3.5 Hz, 1H), 2.46 – 2.39 (m, 2H), 2.35 (s, 3H), 2.38 – 2.33 (m, 1H), 2.30 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.3, 168.0, 151.7, 139.4, 137.4, 132.1, 132.0, 130.4, 129.3, 128.5, 127.6, 121.0, 118.4, 49.0, 40.2, 36.3, 29.5, 24.9, 21.2; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{23}H_{23}N_2O_2^+$ 359.1754; Found 359.1753.

N-(5-([1,1'-Biphenyl]-4-ylmethyl)-2-benzoyl-5-cyanocyclopent-1-en-1-yl)acetamide (2c):



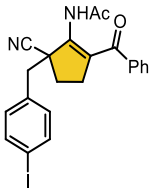
Prepared according to the general procedure as described above in 12 h with 84% yield (71 mg). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.4) to afford a pale yellowish solid; mp = 107-109 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.69 (s, 1H), 7.62 – 7.56 (m, 4H), 7.51 – 7.40 (m, 7H), 7.36 (t, *J* = 7.4 Hz, 3H), 3.65 (d, *J* = 13.3 Hz, 1H), 3.34 (d, *J* = 13.3 Hz, 1H), 2.55 – 2.47 (m, 1H), 2.47 – 2.43 (m, 1H), 2.43 – 2.34 (m, 2H), 2.33 (s, 3H); ^{13}C NMR (176 MHz, $CDCl_3$) δ 195.4, 168.1, 151.6, 140.7, 139.4, 134.1, 132.2, 131.0, 129.0, 128.5, 127.6, 127.3, 127.2, 121.0 (2C), 118.5, 118.4, 48.9, 40.4, 36.4, 29.5, 25.0; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{28}H_{25}N_2O_2^+$ 421.1911; Found 421.1910.

***N*-(2-Benzoyl-5-cyano-5-(4-fluorobenzyl)cyclopent-1-en-1-yl)acetamide (2d):**



Prepared according to the general procedure as described above in 12 h with 68% yield (49 mg). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.4) to afford a pink solid; mp = 155-157 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.70 (s, 1H), 7.51 (ddd, *J* = 7.2, 6.5, 2.0 Hz, 3H), 7.46 – 7.39 (m, 2H), 7.34 (dd, *J* = 8.5, 5.4 Hz, 2H), 7.04 (t, *J* = 8.6 Hz, 2H), 3.65 (d, *J* = 13.4 Hz, 1H), 3.11 (d, *J* = 13.5 Hz, 1H), 2.59 (ddd, *J* = 14.9, 8.7, 3.2 Hz, 1H), 2.50 (ddd, *J* = 10.7, 8.9, 4.8 Hz, 1H), 2.37 (ddd, *J* = 13.3, 7.0, 3.3 Hz, 1H), 2.31 (s, 3H), 2.33 – 2.18 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 195.3, 168.2, 162.5 (d, *J* = 246.5 Hz), 151.9, 139.3, 132.3, 132.1 (d, *J* = 8.0 Hz), 130.9 (d, *J* = 2.9 Hz), 128.6, 127.6, 120.7, 118.1, 115.6 (d, *J* = 21.4 Hz), 49.0, 39.5, 36.2, 29.4, 24.9 ^{19}F NMR (376 MHz, $CDCl_3$) δ -114.76 (s, 1F); HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{22}H_{20}FN_2O_2^+$ 363.1503; Found 363.1501.

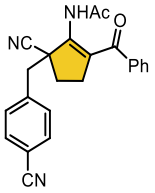
***N*-(2-Benzoyl-5-cyano-5-(4-iodobenzyl)cyclopent-1-en-1-yl)acetamide (2e):**



Prepared according to the general procedure as described above in 12 h with 67% yield (63 mg). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.4) to afford a pink semi-

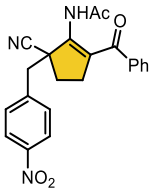
solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.66 (s, 1H), 7.69 (d, *J* = 8.2 Hz, 2H), 7.52 (ddd, *J* = 6.8, 5.3, 2.1 Hz, 1H), 7.49 – 7.40 (m, 4H), 7.11 (d, *J* = 8.3 Hz, 2H), 3.60 (d, *J* = 13.3 Hz, 1H), 3.14 (d, *J* = 13.3 Hz, 1H), 2.56 (ddd, *J* = 14.9, 8.1, 3.4 Hz, 1H), 2.50 – 2.41 (m, 1H), 2.38 – 2.34 (m, 1H), 2.34 – 2.29 (m, 1H), 2.31 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 195.4, 168.2, 151.6, 139.3, 137.8, 134.8, 132.5, 132.3, 128.6, 127.6, 120.6, 118.4, 93.5, 48.8, 40.1, 36.3, 29.5, 25.0; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{22}H_{20}IN_2O_2^+$ 471.0564; Found 471.0562.

***N*-(2-Benzoyl-5-cyano-5-(4-cyanobenzyl)cyclopent-1-en-1-yl)acetamide (2f):**



Prepared according to the general procedure as described above in 48 h with 82% yield (60 mg). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.3) to afford a yellowish orange semi-solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.72 (s, 1H), 7.66 (d, *J* = 8.0 Hz, 2H), 7.54 (dd, *J* = 9.5, 3.9 Hz, 5H), 7.48 – 7.41 (m, 2H), 3.82 (d, *J* = 13.1 Hz, 1H), 3.06 (d, *J* = 13.2 Hz, 1H), 2.77 – 2.57 (m, 2H), 2.31 (s, 3H), 2.38 – 2.27 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.2, 168.4, 151.7, 140.7, 139.2, 132.5, 132.4, 131.3, 128.7, 127.6, 120.1, 118.6, 118.1, 111.8, 48.8, 40.0, 36.3, 29.3, 24.9; IR (neat): υmax 3305, 3018, 2927, 2857, 2229, 1710, 1625, 1580, 1566, 1449, 1263, 749 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{23}H_{20}N_3O_2^+$ 370.1550; Found 370.1547.

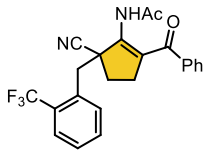
***N*-(2-Benzoyl-5-cyano-5-(4-nitrobenzyl)cyclopent-1-en-1-yl)acetamide (2g):**



Prepared according to the general procedure as described above in 48 h with 85% yield (66 mg). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.3) to afford a reddish brown solid; mp = 168-170 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.74 (s, 1H), 8.22 (d, *J* = 8.6 Hz, 2H), 7.56 (ddd, *J* = 13.8, 11.7, 8.0 Hz, 5H), 7.44 (t, *J* = 7.5 Hz, 2H), 3.88 (d, *J* = 13.1 Hz, 1H), 3.07 (d,

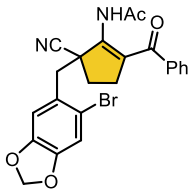
J = 13.1 Hz, 1H), 2.71 (t, *J* = 6.4 Hz, 2H), 2.38 – 2.26 (m, 2H), 2.32 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.2, 168.4, 151.7, 147.7, 142.8, 139.2, 132.5, 131.5, 128.6, 127.6, 123.8, 120.0, 118.0, 48.8, 39.5, 36.3, 29.3, 24.9; IR (neat): υmax 3213, 3017, 2927, 2856, 2240, 1710, 1626, 1581, 1567, 1520, 1450, 1346, 1265 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{22}H_{20}N_3O_4^+$ 390.1448; Found 390.1447.

_N_-(2-Benzoyl-5-cyano-5-(2-(trifluoromethyl)benzyl)cyclopent-1-en-1-yl)acetamide (2h):



Prepared according to the general procedure as described above in 24 h with 86% yield (67 mg). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.3) to afford a yellowish orange solid; mp = 137-139 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.81 (s, 1H), 7.98 (d, *J* = 7.8 Hz, 1H), 7.70 (d, *J* = 7.9 Hz, 1H), 7.63 – 7.56 (m, 3H), 7.56 – 7.51 (m, 1H), 7.48 – 7.39 (m, 3H), 3.98 (d, *J* = 14.6 Hz, 1H), 3.29 (d, *J* = 14.6 Hz, 1H), 2.74 – 2.62 (m, 2H), 2.32 (s, 3H), 2.29 – 2.20 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.4, 168.3, 152.4, 139.4, 134.2, 132.6, 132.3, 132.2, 129.4 (q, J_{CF} = 28.9 Hz), 128.6, 127.7, 127.6, 126.5 (q, J_{CF} = 5.6 Hz), 124.6 (q, J_{CF} = 273.8 Hz), 121.3, 117.9, 48.9, 35.9, 34.7, 29.3, 25.0; ^{19}F NMR (376 MHz, $CDCl_3$) δ -57.25 (s, 3F); IR (neat): υmax 3296, 3016, 2927, 2870, 2239, 1712, 1625, 1580, 1566, 1450, 1310, 1263, 1111, 752 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{23}H_{20}F_3N_2O_2^+$ 413.1471; Found 413.1470.

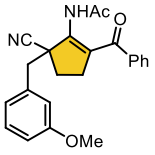
_N_-(2-Benzoyl-5-((6-bromobenzo[*d*][1,3]dioxol-5-yl)methyl)-5-cyanocyclopent-1-en-1-yl)acetamide (2i):



Prepared according to the general procedure as described above in 24 h with 76% yield (71 mg). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.3) to afford a pink solid; mp = 159-161 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.81 (s, 1H), 7.64 – 7.58 (m, 2H), 7.57 – 7.51 (m, 1H), 7.45 (t, *J* = 7.4 Hz, 2H), 7.22 (s, 1H), 7.03 (s, 1H), 5.98 (s, 2H), 3.74 (d, *J* = 13.8 Hz, 1H),

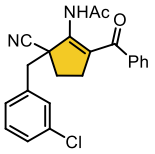
3.29 (d, *J* = 13.8 Hz, 1H), 2.90 (ddd, *J* = 16.0, 9.1, 7.2 Hz, 1H), 2.65 (ddd, *J* = 15.0, 8.6, 1.9 Hz, 1H), 2.52 (ddd, *J* = 13.0, 7.1, 1.8 Hz, 1H), 2.31 (s, 3H), 2.21 (ddd, *J* = 24.8, 14.4, 8.2 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.3, 168.2, 152.4, 148.2, 147.8, 139.5, 132.3, 128.6, 128.0, 127.7, 120.8, 117.7, 116.2, 112.7, 112.0, 102.1, 49.7, 38.0, 35.7, 29.8, 25.0; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{23}H_{20}BrO_4N_2^+$ 467.0601; Found 467.0593

***N*-(2-Benzoyl-5-cyano-5-(3-methoxybenzyl)cyclopent-1-en-1-yl)acetamide (2j):**



Prepared according to the general procedure as described above in 12 h with 68% yield (51 mg). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.4) to afford a reddish brown semi-solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 11.65 (s, 1H), 7.56 – 7.49 (m, 3H), 7.44 (t, *J* = 7.6 Hz, 2H), 7.28 (t, *J* = 3.9 Hz, 1H), 6.94 (t, *J* = 5.1 Hz, 2H), 6.90 – 6.87 (m, 1H), 3.82 (s, 3H), 3.66 (d, *J* = 13.3 Hz, 1H), 3.17 (d, *J* = 13.3 Hz, 1H), 2.58 (ddd, *J* = 14.7, 8.8, 2.7 Hz, 1H), 2.53 – 2.46 (m, 1H), 2.42 (ddd, *J* = 13.0, 7.1, 2.7 Hz, 1H), 2.37 – 2.29 (m, 1H), 2.32 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.4, 168.1, 159.7, 151.8, 139.4, 136.6, 132.2, 129.6, 128.5, 127.6, 122.9, 121.0, 118.4, 116.0, 113.3, 55.4, 48.9, 40.6, 36.3, 29.5, 24.9; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{23}H_{23}N_2O_3^+$ 375.1703; Found 375.1702.

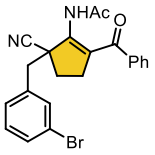
***N*-(2-Benzoyl-5-(3-chlorobenzyl)-5-cyanocyclopent-1-en-1-yl)acetamide (2k):**



Prepared according to the general procedure as described above in 12 h with 81% yield (61 mg). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.4) to afford a pink semisolid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.70 (s, 1H), 7.55 – 7.49 (m, 3H), 7.46 – 7.40 (m, 2H), 7.32 (d, *J* = 9.5 Hz, 4H), 3.67 (d, *J* = 13.3 Hz, 1H), 3.10 (d, *J* = 13.3 Hz, 1H), 2.61 (ddd, *J* = 14.9, 8.4, 3.2 Hz, 1H), 2.52 (dt, *J* = 15.0, 7.6 Hz, 1H), 2.38 – 2.30 (m, 2H), 2.32 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.3, 168.2, 151.8, 139.3, 137.2, 134.4, 132.3, 130.5, 130.0, 128.8, 128.6, 128.0, 127.6,

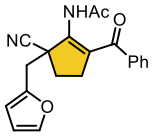
120.5, 118.2, 48.8, 39.9, 36.3, 29.5, 25.0; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{22}H_{20}ClN_2O_2^+$ 379.1208; Found 379.1206.

***N*-(2-Benzoyl-5-(3-bromobenzyl)-5-cyanocyclopent-1-en-1-yl)acetamide (2l):**



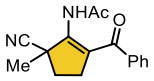
Prepared according to the general procedure as described above in 12 h with 76% yield (64 mg). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.4) to afford a pink solid; mp = 155-157 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ 11.70 (s, 1H), 7.56 – 7.49 (m, 3H), 7.49 – 7.45 (m, 2H), 7.45 – 7.41 (m, 2H), 7.36 (d, *J* = 7.7 Hz, 1H), 7.24 (t, *J* = 7.7 Hz, 1H), 3.66 (d, *J* = 13.4 Hz, 1H), 3.10 (d, *J* = 13.4 Hz, 1H), 2.61 (ddd, *J* = 15.0, 8.4, 3.2 Hz, 1H), 2.56 – 2.48 (m, 1H), 2.37 (ddd, *J* = 11.4, 6.2, 2.3 Hz, 1H), 2.35 – 2.29 (m, 1H), 2.31 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 195.3, 168.2, 151.8, 139.3, 137.5, 133.4, 132.3, 130.9, 130.3, 129.3, 128.6, 127.6, 122.6, 120.5, 118.2, 48.8, 39.9, 36.3, 29.5, 25.0; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{22}H_{20}BrN_2O_2^+$ 423.0703; Found 423.0700.

***N*-(2-Benzoyl-5-cyano-5-(furan-2-ylmethyl)cyclopent-1-en-1-yl)acetamide (2m):**



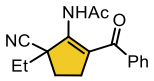
Prepared according to the general procedure as described above in 12 h with 86% yield (57 mg). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.4) to afford a colorless oil; ^1H NMR (400 MHz, $CDCl_3$) δ 11.61 (s, 1H), 7.57 – 7.48 (m, 3H), 7.45 – 7.40 (m, 2H), 7.39 (dd, *J* = 1.8, 0.7 Hz, 1H), 6.37 (dd, *J* = 3.2, 1.9 Hz, 1H), 6.28 (d, *J* = 3.1 Hz, 1H), 3.61 (d, *J* = 14.8 Hz, 1H), 3.50 (d, *J* = 14.8 Hz, 1H), 2.66 – 2.57 (m, 1H), 2.56 – 2.47 (m, 2H), 2.43 (ddd, *J* = 15.5, 7.7, 4.6 Hz, 1H), 2.28 (s, 3H); ^{13}C NMR (176 MHz, $CDCl_3$) δ 195.3, 168.2, 151.0, 149.7, 142.6, 139.4, 132.2, 128.5, 127.6, 120.7, 118.7, 111.0, 109.6, 48.2, 36.9, 33.9, 29.4, 24.9; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{20}H_{19}N_2O_3^+$ 335.1396; Found 335.1399.

***N*-(2-benzoyl-5-cyano-5-methylcyclopent-1-en-1-yl)acetamide (2n):**



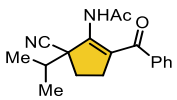
Prepared according to the general procedure as described above in 12 h with 93% yield (50 g). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.4) to afford a reddish-orange solid; mp = 115-117 ^oC; ^1H NMR (400 MHz, $CDCl_3$) δ 11.59 (s, 1H), 7.67 – 7.60 (m, 2H), 7.56 – 7.50 (m, 1H), 7.44 (t, *J* = 7.4 Hz, 2H), 2.95 – 2.74 (m, 2H), 2.57 (dt, *J* = 12.8, 7.8 Hz, 1H), 2.23 (s, 3H), 2.22 – 2.14 (m, 1H), 1.77 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.3, 167.9, 153.4, 139.4, 132.2, 128.5, 127.7, 121.8, 117.1, 43.5, 40.3, 29.3, 24.8, 22.9; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{16}H_{16}N_2O_2^+$ 269.1285; Found 269.1284.

***N*-(2-Benzoyl-5-cyano-5-ethylcyclopent-1-en-1-yl)acetamide (2o):**



Prepared according to the general procedure as described above in 12 h with 91% yield (51 g). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.4) to afford a reddish solid; mp = 125-127 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ 11.56 (s, 1H), 7.63 (dt, *J* = 8.4, 1.6 Hz, 2H), 7.56 – 7.50 (m, 1H), 7.48 – 7.42 (m, 2H), 2.81 (dd, *J* = 7.9, 6.0 Hz, 2H), 2.49 – 2.41 (m, 1H), 2.41 – 2.33 (m, 1H), 2.32 – 2.25 (m, 1H), 2.22 (s, 3H), 1.74 (dq, *J* = 14.7, 7.4 Hz, 1H), 1.16 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.3, 167.9, 152.4, 139.4, 132.2, 128.5, 127.7, 120.8, 117.7, 49.0, 36.3, 29.6, 27.8, 24.8, 9.8; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{17}H_{19}O_2N_2^+$ 283.1441; Found 283.1441.

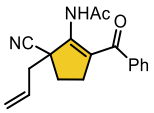
***N*-(2-Benzoyl-5-cyano-5-isopropylcyclopent-1-en-1-yl)acetamide (2p):**



Prepared according to the general procedure as described above in 12 h with 90% yield (53 mg). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.4) to afford a yellowish orange solid; mp = 161-163 ^oC; ^1H NMR (400 MHz, $CDCl_3$) δ 11.29 (s, 1H), 7.62 (dd, *J* = 5.2, 3.3 Hz, 2H), 7.56 – 7.49 (m, 1H), 7.44 (dd, *J* = 10.2, 4.6 Hz, 2H), 2.98 – 2.84 (m, 2H), 2.76 – 2.64 (m,

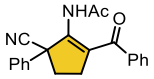
1H), 2.38 – 2.24 (m, 2H), 2.19 (s, 3H), 1.19 (d, *J* = 6.8 Hz, 3H), 0.89 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.4, 167.9, 149.7, 139.4, 132.2, 128.5, 127.7, 121.6, 120.0, 53.1, 31.6, 30.8, 30.5, 24.8, 18.8, 16.3; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{18}H_{21}N_2O_2^+$ 297.1603; Found 297.1598.

***N*-(5-Allyl-2-benzoyl-5-cyanocyclopent-1-en-1-yl)acetamide (2q):**



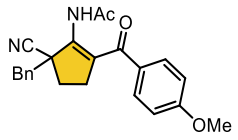
Prepared according to the general procedure as described above in 12 h with 88% yield (52 mg). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.4) to afford a yellowish orange semi solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.59 (s, 1H), 7.63 (d, *J* = 7.4 Hz, 2H), 7.53 (t, *J* = 7.1 Hz, 1H), 7.45 (t, *J* = 7.4 Hz, 2H), 5.99 – 5.78 (m, 1H), 5.33 – 5.23 (m, 2H), 3.11 (dd, *J* = 13.5, 6.4 Hz, 1H), 2.80 (t, *J* = 7.3 Hz, 2H), 2.57 (dd, *J* = 13.4, 8.0 Hz, 1H), 2.39 (ddd, *J* = 21.2, 14.2, 8.2 Hz, 2H), 2.24 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.3, 168.0, 151.9, 139.5, 132.3, 131.7, 128.6, 127.7, 120.8, 120.7, 118.1, 47.7, 39.1, 36.4, 29.6, 24.8; IR (neat): υmax 3292, 3065, 3018, 2925, 2856, 2239, 1711, 1624, 1580, 1566, 1448, 1267, 697 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{18}H_{19}N_2O_2^+$ 295.1441; Found 295.1440.

***N*-(2-benzoyl-5-cyano-5-phenylcyclopent-1-en-1-yl)acetamide (2r):**



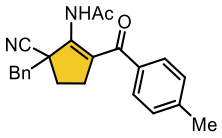
Prepared according to the general procedure as described above in 12 h with 89% yield (59 mg). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.4) to afford a pink semi-solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 11.32 (s, 1H), 7.76 – 7.71 (m, 2H), 7.59 – 7.54 (m, 1H), 7.48 (dd, *J* = 10.4, 4.6 Hz, 2H), 7.43 – 7.37 (m, 4H), 7.34 – 7.28 (m, 1H), 3.09 – 3.00 (m, 1H), 2.91 – 2.82 (m, 2H), 2.34 (ddd, *J* = 14.7, 8.5, 6.2 Hz, 1H), 2.02 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.9, 166.9, 150.3, 139.3, 138.2, 132.4, 129.1, 128.6, 127.9, 127.9, 125.2, 120.2, 120.1, 54.1, 44.0, 30.0, 24.3; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{21}H_{19}N_2O_2^+$ 331.1441; Found 331.1439.

***N*-(5-Benzyl-5-cyano-2-(4-methoxybenzoyl)cyclopent-1-en-1-yl)acetamide (2s):**



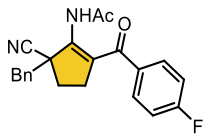
Prepared according to the general procedure as described above in 12 h with 85% yield (64 mg). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.4) to afford a yellowish orange semisolid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 11.62 (s, 1H), 7.51 (dt, *J* = 8.9, 2.9 Hz, 2H), 7.37 – 7.29 (m, 5H), 6.89 (dt, *J* = 8.8, 2.9 Hz, 2H), 3.85 (s, 3H), 3.62 (d, *J* = 13.3 Hz, 1H), 3.22 (d, *J* = 13.4 Hz, 1H), 2.58 (ddd, *J* = 14.4, 8.7, 2.5 Hz, 1H), 2.50 – 2.42 (m, 1H), 2.40 (ddd, *J* = 12.9, 7.1, 2.6 Hz, 1H), 2.34 – 2.29 (m, 1H), 2.28 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.5, 168.1, 163.0, 150.9, 135.2, 131.8, 130.5, 130.3, 128.6, 127.6, 121.1, 119.0, 113.7, 55.6, 48.8, 40.6, 36.5, 29.9, 24.8; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{23}H_{23}N_2O_3^+$ 375.1703; Found 375.1700.

***N*-(5-Benzyl-5-cyano-2-(4-methylbenzoyl)cyclopent-1-en-1-yl)acetamide (2t):**



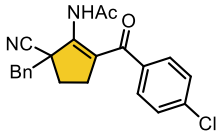
Prepared according to the general procedure as described above in 12 h with 77% yield (55 mg). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.4) to afford a pink solid; mp = 143-145 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 11.67 (s, 1H), 7.38 (d, *J* = 8.2 Hz, 2H), 7.36 – 7.31 (m, 5H), 7.20 (d, *J* = 7.9 Hz, 2H), 3.62 (d, *J* = 13.3 Hz, 1H), 3.23 (d, *J* = 13.3 Hz, 1H), 2.53 (ddd, *J* = 13.3, 8.7, 3.5 Hz, 1H), 2.43 (dd, *J* = 13.6, 5.7 Hz, 1H), 2.41 – 2.37 (m, 1H), 2.39 (s, 3H), 2.34 – 2.28 (m, 1H), 2.30 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 194.9, 168.1, 151.4, 143.0, 136.7, 135.2, 130.5, 129.2, 128.6, 127.9, 127.6, 121.0, 118.7, 48.8, 40.6, 36.4, 29.6, 24.9, 21.7; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{23}H_{23}N_2O_2^+$ 359.1754; Found 359.1751.

***N*-(5-Benzyl-5-cyano-2-(4-fluorobenzoyl)cyclopent-1-en-1-yl)acetamide (2u):**



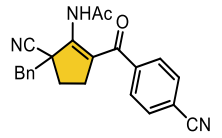
Prepared according to the general procedure as described above in 12 h with 79% yield (57 mg). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.4) to afford an light orange solid; mp = 111-113 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.52 (s, 1H), 7.52 – 7.46 (m, 2H), 7.36 – 7.32 (m, 5H), 7.11 – 7.04 (m, 2H), 3.60 (d, *J* = 13.3 Hz, 1H), 3.26 (d, *J* = 13.3 Hz, 1H), 2.51 (ddd, *J* = 12.0, 9.8, 5.6 Hz, 1H), 2.47 – 2.38 (m, 2H), 2.38 – 2.31 (m, 1H), 2.29 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 193.6, 168.0, 165.0 (d, *J* = 254.1 Hz), 151.6, 135.5 (d, *J* = 3.0 Hz), 135.1, 130.5, 130.3 (d, *J* = 9.1 Hz), 128.6, 127.7, 120.9, 118.3, 115.7 (d, *J* = 21.9 Hz), 48.8, 40.6, 36.3, 29.6, 24.9; ^{19}F NMR (377 MHz, $CDCl_3$) δ -105.98 (s, 1F); HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{22}H_{20}FN_2O_2^+$ 363.1503; Found 363.1504.

***N*-(5-Benzyl-2-(4-chlorobenzoyl)-5-cyanocyclopent-1-en-1-yl)acetamide (2v):**



Prepared according to the general procedure as described above in 12 h with 82% yield (62 mg). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.4) to afford a yellowish orange semisolid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.54 (s, 1H), 7.41 – 7.36 (m, 4H), 7.34 (s, 5H), 3.59 (d, *J* = 13.3 Hz, 1H), 3.26 (d, *J* = 13.3 Hz, 1H), 2.48 (ddd, *J* = 14.1, 7.9, 2.7 Hz, 1H), 2.44 – 2.38 (m, 1H), 2.38 – 2.31 (m, 2H), 2.30 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 193.8, 168.0, 151.9, 138.6, 137.6, 135.0, 130.5, 129.2, 128.8, 128.7, 127.7, 120.9, 118.2, 48.9, 40.7, 36.3, 29.5, 24.9; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{22}H_{18}ClN_2O_2^+$ 377.1057; Found 377.1074.

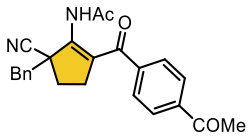
***N*-(2-Benzoyl-5-benzyl-5-cyanocyclopent-1-en-1-yl)-2-chloroacetamide (2w):**



Prepared according to the general procedure as described above in 48 h with 61% yield (45 mg). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.3) to afford a pink solid; mp = 124-126 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.47 (s, 1H), 7.70 (d, *J* = 8.1 Hz, 2H), 7.49 (d, *J* = 8.0 Hz, 2H), 7.34 (s, 5H), 3.57 (d, *J* = 13.3 Hz, 1H), 3.29 (d, *J* = 13.4 Hz, 1H), 2.48 – 2.39 (m, 2H), 2.39 – 2.34 (m, 1H), 2.33 – 2.29 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.4, 168.0, 152.7,

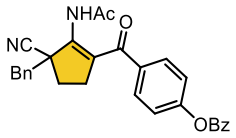
142.8, 134.8, 132.4, 130.5, 128.7, 128.0, 127.8, 120.6, 117.9, 117.5, 115.4, 48.9, 40.8, 36.1, 29.2, 25.0; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{23}H_{20}N_3O_2^+$ 370.1550; Found 370.1548.

***N*-(2-(4-Acetylbenzoyl)-5-benzyl-5-cyanocyclopent-1-en-1-yl)acetamide (2x):**



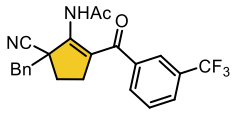
Prepared according to the general procedure as described above in 36 h with 65% yield (50 mg). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.3) to afford a yellowish orange semi-solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.61 (s, 1H), 7.97 (d, *J* = 8.4 Hz, 2H), 7.48 (d, *J* = 8.4 Hz, 2H), 7.34 (s, 5H), 3.59 (d, *J* = 13.3 Hz, 1H), 3.29 (d, *J* = 13.4 Hz, 1H), 2.63 (s, 3H), 2.49 – 2.39 (m, 2H), 2.39 – 2.30 (m, 2H), 2.32 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.4, 194.5, 168.0, 152.4, 143.0, 139.3, 135.0, 130.6, 128.7, 128.4, 127.8, 127.7, 120.8, 117.9, 48.9, 40.8, 36.2, 29.2, 26.9, 25.0; IR (neat): υmax 3305, 3018, 2926, 2855, 2239, 1714, 1686, 1623, 1574, 1456, 1262, 703 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{24}H_{23}N_2O_3^+$ 387.1703; Found 387.1703.

4-(2-acetamido-3-benzyl-3-cyanocyclopent-1-ene-1-carbonyl)phenyl benzoate (2y):



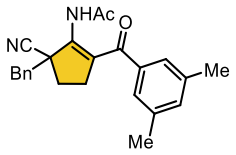
Prepared according to the general procedure as described above in 36 h with 69% yield (64 mg). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.3) to afford a reddish semisolid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.63 (s, 1H), 8.20 (dd, *J* = 8.3, 1.2 Hz, 2H), 7.67 (ddd, *J* = 7.0, 2.5, 1.3 Hz, 1H), 7.57 – 7.50 (m, 4H), 7.39 – 7.32 (m, 5H), 7.31 – 7.26 (m, 2H), 3.61 (d, *J* = 13.3 Hz, 1H), 3.28 (d, *J* = 13.3 Hz, 1H), 2.60 – 2.52 (m, 1H), 2.44 (ddd, *J* = 11.5, 5.8, 4.1 Hz, 2H), 2.40 – 2.36 (m, 1H), 2.32 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.0, 168.1, 164.8, 153.9, 151.8, 136.9, 135.1, 134.1, 130.6, 130.4, 129.4, 129.1, 128.8, 128.7, 127.7, 121.9, 121.0, 118.4, 48.9, 40.7, 36.4, 29.6, 25.0; IR (neat): υmax 3290, 3064, 3028, 2918, 2850, 2240, 1737, 1702, 1622, 1584, 1452, 1203, 705 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{29}H_{25}N_2O_4^+$ 465.1809; Found 465.1807.

***N*-(5-Benzyl-5-cyano-2-(3-(trifluoromethyl)benzoyl)cyclopent-1-en-1-yl)acetamide (2z):**



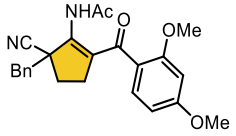
Prepared according to the general procedure as described above in 24 h with 88% yield (72 mg). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.3) to afford a colorless semisolid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.57 (s, 1H), 7.75 (d, *J* = 7.6 Hz, 1H), 7.66 – 7.58 (m, 2H), 7.58 – 7.51 (m, 1H), 7.38 – 7.31 (m, 5H), 3.56 (d, *J* = 13.4 Hz, 1H), 3.36 (d, *J* = 13.4 Hz, 1H), 2.46 (dt, *J* = 10.3, 4.1 Hz, 1H), 2.40 (ddd, *J* = 13.5, 6.0, 2.3 Hz, 2H), 2.32 (s, 3H), 2.31 – 2.23 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 193.6, 168.0, 152.5, 131.1 (q, J_{CF} = 33.0 Hz), 140.0, 134.9, 130.7, 130.6, 129.2, 128.7, 128.5 (q, J_{CF} = 3.3 Hz), 127.9, 124.5 (q, J_{CF} = 3.7 Hz), 123.7 (q, J_{CF} = 272.9 Hz), 120.8, 117.7, 48.9, 40.9, 36.3, 29.3, 25.0; ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.79 (s, 3F); HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{23}H_{20}F_3N_2O_2^+$ 413.1471; Found 413.1469.

***N*-(5-Benzyl-5-cyano-2-(3,5-dimethylbenzoyl)cyclopent-1-en-1-yl)acetamide (2aa):**



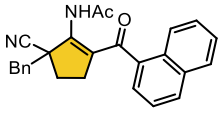
Prepared according to the general procedure as described above in 12 h with 76% yield (56 mg). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.4) to afford a yellowish orange semisolid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.68 (s, 1H), 7.37 – 7.32 (m, 5H), 7.12 (s, 1H), 7.00 (s, 2H), 3.60 (d, *J* = 13.3 Hz, 1H), 3.30 (d, *J* = 13.3 Hz, 1H), 2.51 – 2.44 (m, 1H), 2.43 – 2.38 (m, 1H), 2.38 – 2.33 (m, 2H), 2.32 (s, 6H), 2.31 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 195.9, 168.1, 151.3, 139.6, 138.2, 135.3, 133.8, 130.6, 128.6, 127.7, 125.2, 121.1, 118.7, 48.8, 40.8, 36.4, 29.6, 24.9, 21.3; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{24}H_{25}N_2O_2^+$ 373.1911; Found 373.1913.

***N*-(5-Benzyl-5-cyano-2-(2,4-dimethoxybenzoyl)cyclopent-1-en-1-yl)acetamide (2ab):**



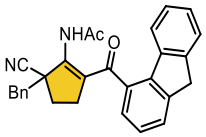
Prepared according to the general procedure as described above in 12 h with 80% yield (65 mg). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.4) to afford a brownish semisolid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.66 (s, 1H), 7.37 – 7.28 (m, 5H), 7.07 (d, *J* = 8.4 Hz, 1H), 6.47 (dd, *J* = 8.4, 2.2 Hz, 1H), 6.43 (d, *J* = 2.2 Hz, 1H), 3.83 (s, 3H), 3.78 (s, 3H), 3.65 (d, *J* = 13.3 Hz, 1H), 3.07 (d, *J* = 13.3 Hz, 1H), 2.47 – 2.34 (m, 1H), 2.32 (dd, *J* = 5.9, 2.8 Hz, 1H), 2.29 (s, 3H), 2.28 – 2.20 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.7, 168.0, 163.3, 158.1, 150.1, 135.3, 130.5, 130.0, 128.5, 127.5, 123.1, 121.1, 120.2, 104.8, 98.7, 55.6, 49.1, 40.3, 35.8, 27.6, 24.9; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{24}H_{25}N_2O_4^+$ 405.1809; Found 405.1809.

***N*-(2-(1-Naphthoyl)-5-benzyl-5-cyanocyclopent-1-en-1-yl)acetamide (2ac):**



Prepared according to the general procedure as described above in 12 h with 59% yield (46 mg). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.4) to afford a reddish semisolid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.96 (s, 1H), 7.93 – 7.85 (m, 2H), 7.71 – 7.63 (m, 1H), 7.55 – 7.47 (m, 2H), 7.44 (dd, *J* = 8.2, 7.1 Hz, 1H), 7.38 – 7.30 (m, 5H), 7.18 (dd, *J* = 7.1, 1.0 Hz, 1H), 3.57 (d, *J* = 13.3 Hz, 1H), 3.39 (d, *J* = 13.3 Hz, 1H), 2.39 (s, 3H), 2.37 – 2.29 (m, 2H), 2.13 (ddd, *J* = 15.3, 8.1, 3.4 Hz, 1H), 2.05 – 1.95 (m, 1H); ^{13}C NMR (176 MHz, $CDCl_3$) δ 198.1, 168.1, 151.7, 137.8, 135.0, 133.6, 130.9, 130.6, 130.3, 129.1, 128.7, 127.7, 127.5, 126.7, 124.8, 124.7, 124.4, 121.1, 118.9, 49.0, 41.0, 35.9, 28.5, 25.1; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{26}H_{23}N_2O_2^+$ 395.1754; Found 395.1749.

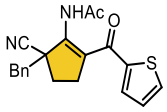
***N*-(5-Benzyl-5-cyano-2-(9*H*-fluorene-4-carbonyl)cyclopent-1-en-1-yl)acetamide (2ad):**



Prepared according to the general procedure as described above in 12 h with 61% yield (53 mg). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.3) to afford a yellowish semi-solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.65 (s, 1H), 7.86 – 7.81 (m, 1H), 7.78 (d, *J* = 8.0 Hz, 1H), 7.66 (s, 1H), 7.59 (d, *J* = 6.9 Hz, 1H), 7.50 (d, *J* = 8.0 Hz, 1H), 7.46 – 7.39 (m, 2H), 7.38 – 7.34 (m, 5H), 3.93 (s, 2H), 3.64 (d, *J* = 13.3 Hz, 1H), 3.28 (d, *J* = 13.3 Hz, 1H), 2.59 (ddd, *J* = 14.1, 8.8, 4.1 Hz, 1H), 2.46 (tt, *J* = 6.8, 5.7 Hz, 2H), 2.39 – 2.33 (m, 1H), 2.31 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 195.1, 168.1, 151.2, 145.8, 144.4, 143.3, 140.5, 137.6, 135.3, 130.6, 128.7,

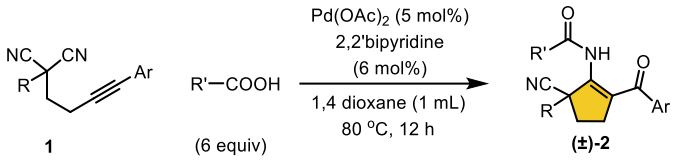
128.2, 127.7, 127.3, 127.0, 125.4, 124.6, 121.1, 120.9, 119.7, 119.0, 48.9, 40.7, 37.0, 36.5, 29.9, 24.9; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{29}H_{25}N_2O_2^+$ 433.1911; Found 433.1909.

***N*-(5-Benzyl-5-cyano-2-(thiophene-2-carbonyl)cyclopent-1-en-1-yl)acetamide (2ae):**



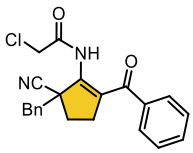
Prepared according to the general procedure as described above in 12 h with 83% yield (58 mg). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.4) to afford a yellowish orange oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.07 (s, 1H), 7.68 (dd, *J* = 5.0, 0.9 Hz, 1H), 7.58 (dd, *J* = 3.9, 0.9 Hz, 1H), 7.43 – 7.27 (m, 5H), 7.13 (dd, *J* = 4.9, 3.9 Hz, 1H), 3.67 (d, *J* = 13.3 Hz, 1H), 3.08 (d, *J* = 13.3 Hz, 1H), 2.88 (ddd, *J* = 14.2, 8.8, 2.6 Hz, 1H), 2.69 – 2.57 (m, 1H), 2.48 (ddd, *J* = 13.1, 7.4, 2.6 Hz, 1H), 2.41 – 2.34 (m, 1H), 2.32 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 184.6, 168.0, 153.3, 145.0, 135.0, 134.5, 132.1, 130.5, 128.6, 128.5, 127.7, 120.8, 116.5, 48.6, 40.4, 36.0, 28.9, 25.1; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{20}H_{19}SN_2O_2^+$ 351.1162; Found 351.1156.

b. General procedure for aromatic and aliphatic acids



A dried screw-cap vial was charged with alkyne-tethered malononitrile **1** (0.2 mmol), $Pd(OAc)_2$ (5 mol%, 0.01 mmol), bipyridine (6 mol%, 0.012 mmol) and acid (1.2 mmol, 6 eq) in 1,4 dioxane (1 mL) under N_2 atmosphere at rt. The reaction mixture was stirred at 80 °C in an oil bath for 12 hours (monitored by TLC). After the completion of the reaction, it was cooled to room temperature and quenched with aqueous $NaHCO_3$ (8 mL) solution. The mixture was extracted with EtOAc (3x8 mL) and concentrated under reduced pressure. The residue was directly subjected to flash column chromatography on silica gel (hexanes/ethyl acetate) to afford the desired product **2**.

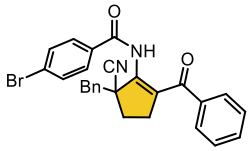
***N*-(2-Benzoyl-5-benzyl-5-cyanocyclopent-1-en-1-yl)-2-chloroacetamide (2af):**



Prepared according to the general procedure as described above in 12 h with 64% yield (48 mg). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.5) to afford a brownish

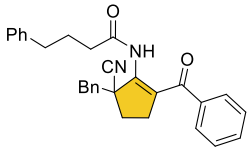
semisolid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 12.21 (s, 1H), 7.52 (dt, *J* = 8.5, 1.2 Hz, 1H), 7.49 – 7.46 (m, 2H), 7.41 (t, *J* = 7.6 Hz, 2H), 7.37 – 7.33 (m, 5H), 4.24 (dd, *J* = 35.2, 15.5 Hz, 2H), 3.59 (d, *J* = 13.4 Hz, 1H), 3.27 (d, *J* = 13.4 Hz, 1H), 2.61 – 2.52 (m, 1H), 2.47 – 2.40 (m, 2H), 2.40 – 2.32 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.2, 164.7, 149.3, 138.9, 134.9, 132.5, 130.5, 128.7, 128.5, 127.8, 121.3, 120.8, 48.8, 42.9, 40.9, 36.3, 29.9; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{22}H_{20}ClN_2O_2^+$ 379.1213; Found 379.1206.

***N*-(2-Benzoyl-5-benzyl-5-cyanocyclopent-1-en-1-yl)-4-bromobenzamide (2ag):**



Prepared according to the general procedure as described above in 12 h with 56% yield (54 mg). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.5) to afford a yellowish orange semisolid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.95 (s, 1H), 8.02 (dt, *J* = 8.7, 2.4 Hz, 2H), 7.70 (dt, *J* = 8.7, 2.3 Hz, 2H), 7.55 – 7.47 (m, 3H), 7.46 – 7.33 (m, 7H), 3.74 (d, *J* = 13.4 Hz, 1H), 3.37 (d, *J* = 13.4 Hz, 1H), 2.62 – 2.54 (m, 1H), 2.51 – 2.42 (m, 2H), 2.42 – 2.32 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 195.8, 163.5, 152.8, 139.4, 135.1, 132.4, 132.3, 131.7, 130.6, 129.8, 128.7, 128.6, 128.2, 127.8, 127.6, 121.0, 119.1, 48.9, 40.9, 36.5, 29.6; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{27}H_{22}BrN_2O_2^+$ 485.0865; Found 485.0866.

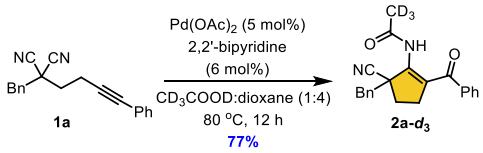
***N*-(2-Benzoyl-5-benzyl-5-cyanocyclopent-1-en-1-yl)-4-phenylbutanamide (2ah):**



Prepared according to the general procedure as described above in 12 h with 52% yield (46 mg). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.5) to afford a colorless semisolid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.65 (s, 1H), 7.53 – 7.47 (m, 1H), 7.46 – 7.38 (m, 4H), 7.36 – 7.27 (m, 7H), 7.25 – 7.17 (m, 3H), 3.62 (d, *J* = 13.3 Hz, 1H), 3.25 (d, *J* = 13.3 Hz, 1H), 2.75 (t, *J* = 7.5 Hz, 2H), 2.59 – 2.46 (m, 3H), 2.43 – 2.35 (m, 2H), 2.31 (tt, *J* = 15.2, 5.4 Hz, 1H), 2.17 – 2.09 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.2, 170.8, 151.8, 141.1, 139.4, 135.1, 132.0, 130.5, 128.6, 128.5, 128.5, 128.4, 127.6, 127.5, 126.1, 120.9, 118.2, 48.8, 40.6, 37.0, 36.3, 35.1, 29.4, 26.6; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{30}H_{28}N_2O_2Na^+$ 471.2048; Found 471.2041.

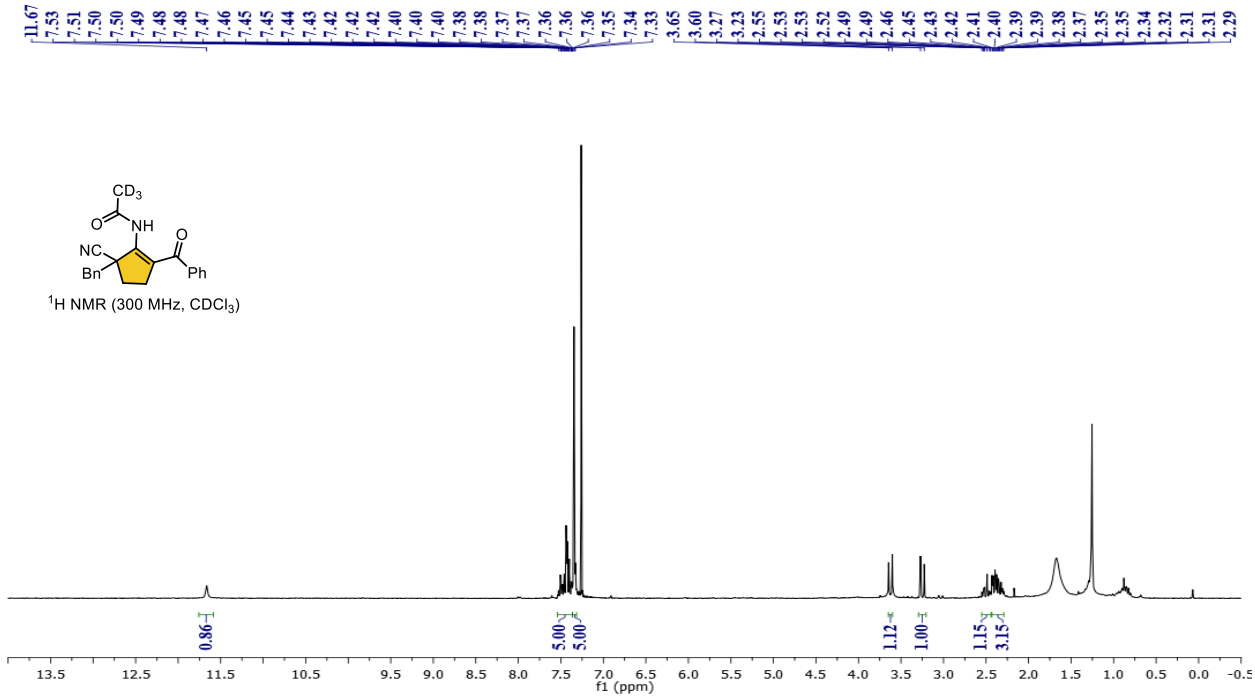
IIIC. Mechanistic studies:

a. Reaction in the presence of CD_3COOD:



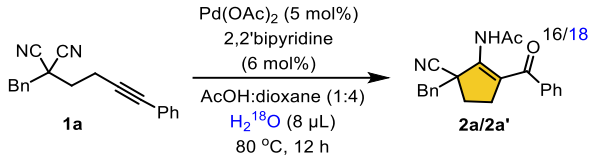
A dried screw-cap vial was charged with alkyne-tethered malononitrile **1a** (25 mg, 0.09 mmol), $Pd(OAc)_2$ (1 mg, 0.004 mmol, 5 mol%), and 2,2'-bipyridine (0.8 mg, 0.005 mmol, 6 mol%) in CD_3COOD:1,4-dioxane (1:4 ratio, 0.5 mL) under N_2 atmosphere at rt. The reaction mixture was stirred at 80 °C in preheated oil bath for 12 hours (monitored by TLC). Then, it was cooled to room temperature and the reaction mixture was directly subjected to flash column chromatography on silica gel (20% EtOAc/hexanes; R_f = 0.4) to afford the desired product **2a-*d*$_3$** as a brownish semisolid (23 mg, 77% yield); ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.67 (s, 1H), 7.54 – 7.36 (m, 5H), 7.36 – 7.31 (m, 5H), 3.62 (d, *J* = 13.3 Hz, 1H), 3.25 (d, *J* = 13.3 Hz, 1H), 2.55 – 2.44 (m, 1H), 2.44 – 2.29 (m, 3H); HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{22}H_{18}D_3N_2O_2^+$ 348.1788; Found 348.1794.

***N*-(2-benzoyl-5-benzyl-5-cyanocyclopent-1-en-1-yl)acetamide-2,2,2-d$_3$ (2a-*d*$_3$):**

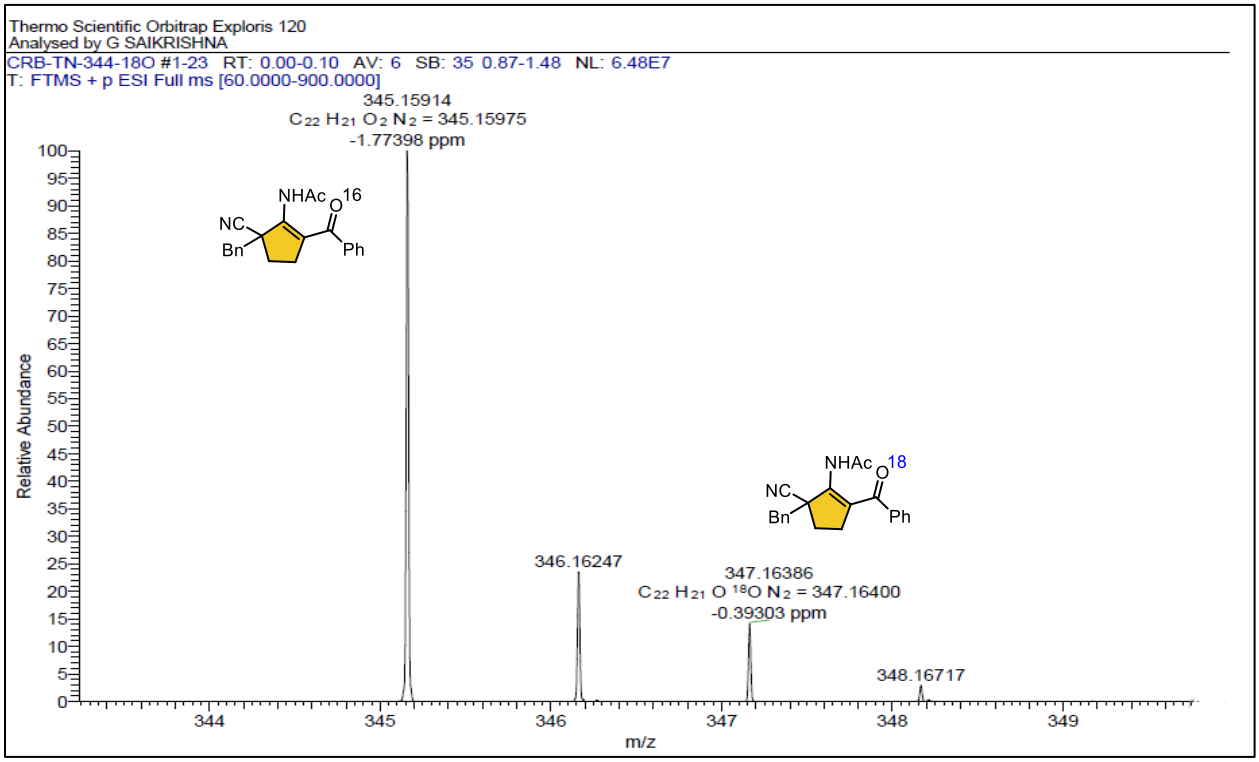


Conclusion: This observation suggests that the reaction may not proceed via a Pd-H pathway.

b. ^{18}O Labelling Studies:

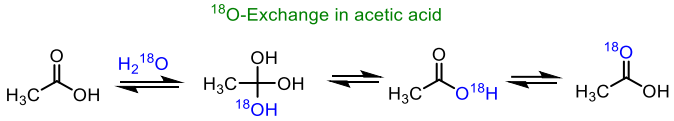


A dried screw-cap vial was charged with alkyne-tethered malononitrile **1a** (25 mg, 0.09 mmol), $Pd(OAc)_2$ (1.0 mg, 0.004 mmol, 5 mol%) and 2,2'-bipyridine (0.8 mg, 0.005 mmol, 6 mol%) in AcOH:1,4-dioxane (1:4 ratio, 0.5 mL) and add $H_2{}^{18}O$ (8 µL, 5 equiv.) under N_2 atmosphere at rt. The reaction mixture was stirred at 80 °C in an oil bath for 12 hours (monitored by TLC). Then, it was cooled to room temperature and the reaction mixture was directly subjected to flash column chromatography on silica gel (20% EtOAc/hexanes; R_f = 0.4) to afford both ^{16}O and ^{18}O labeled products (**2a**, **2a'**) in 74% yield. The ratio of products (7.2:1) were measured by HRMS analysis; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{22}H_{21}N_2{}^{16}O_2{}^+$ 345.1598; Found 345.1591; $[M+H]^+$ Calcd for $C_{22}H_{21}N_2{}^{18}O^{16}O^+$ 347.1640; Found 347.1639.

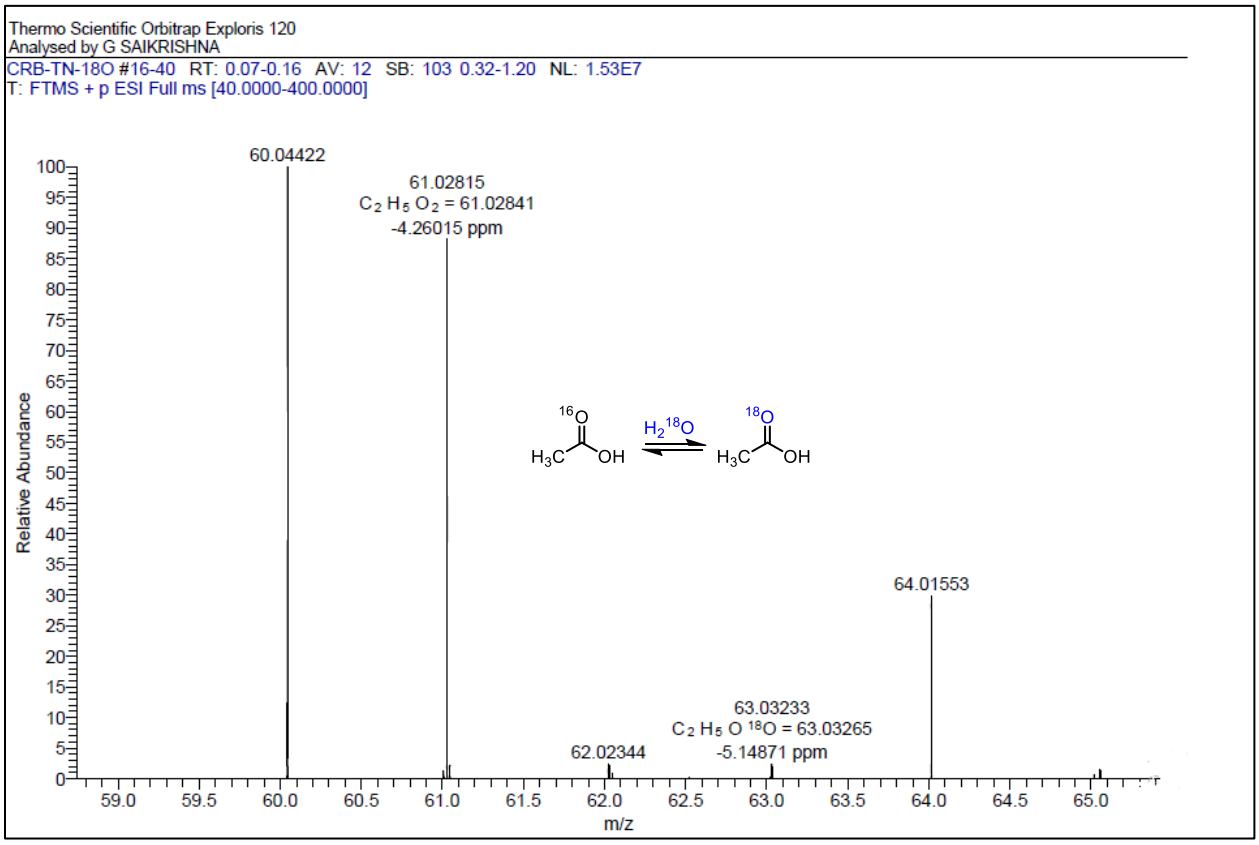


m/z	Intensity	Relative	Theo. Mass	Delta (ppm)	Composition
345.15914	66255436.0	100.00	345.15975	-1.77	$C_{22}H_{21}O_2N_2$
346.16247	15841324.0	23.91			
347.16386	9166873.0	13.84	347.16400	-0.39	$C_{22}H_{21}O\,{}^{18}O\,N_2$

^{18}O Exchange studies in acetic acid:

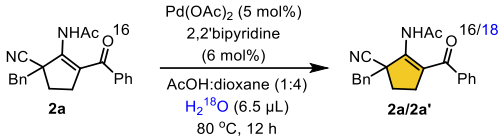


A dried spring bottom vial inserter was charged with acetic acid (90 µL) and $H_2{}^{18}O$ (10 µL). The presence of ^{16}O and ^{18}O labeled acetic acids were measured by ESI analysis; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_2H_5O_2^+$ 61.0284; Found 61.0282; $[M+H]^+$ Calcd for $C_2H_5{}^{18}OO^+$ 63.0327; Found 63.0323.

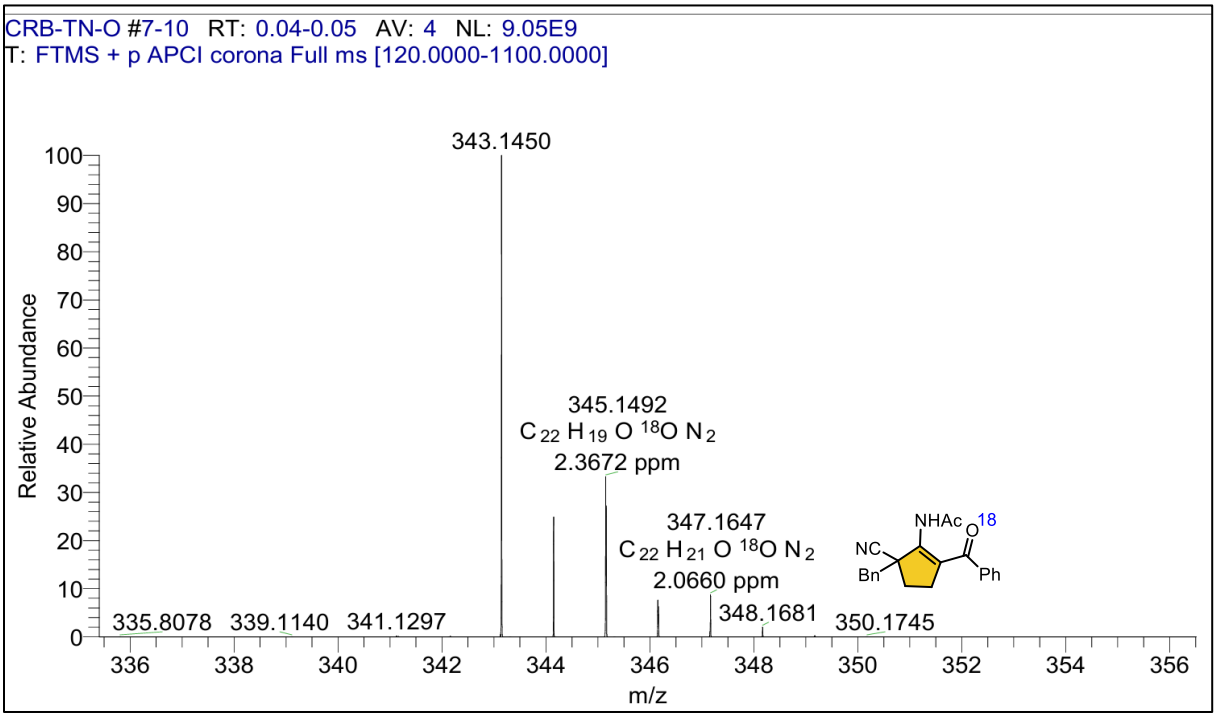


m/z	Intensity	Relative	Theo. Mass	Delta (ppm)	Composition
60.04422	15436404.0	100.00			
61.02815	13528205.0	87.64	61.02841	-4.26	$C_2H_5O_2$
64.01553	4643570.5	30.08			
62.02344	376642.3	2.44			
63.03233	370214.6	2.40	63.03265	-5.15	$C_2H_5O\,{}^{18}O$

^{18}O Exchange study on product 2a :

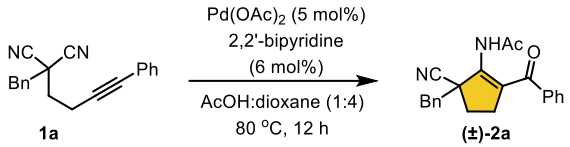


A dried screw-cap vial was charged with enamide **2a** (25 mg, 0.07 mmol), $Pd(OAc)_2$ (0.8 mg, 0.004 mmol, 5 mol%) and 2,2'-bipyridine (0.7 mg, 0.004 mmol, 6 mol%) in AcOH:1,4-dioxane (1:4 ratio, 0.5 mL) and add $H_2{}^{18}O$ (6.5 μL, 5 equiv.) under N_2 atmosphere at rt. The reaction mixture was stirred at 80 ^oC in an oil bath for 12 hours. Then, it was cooled to room temperature and the reaction mixture was directly subjected to flash column chromatography on silica gel (20% EtOAc/hexanes; R_f = 0.4). Trace amount of ^{18}O-labeled product **2a** was observed along with **2a**. HRMS (APCI) m/z: $[M+H]^+$ Calcd for $C_{22}H_{21}N_2{}^{18}OO^+$ 347.1640; Found 347.1647.



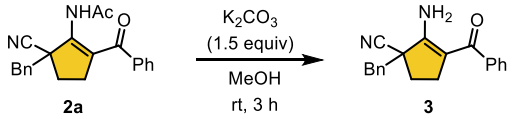
Conclusion: To gain further insights into the reaction mechanism, we conducted an ^{18}O labelling study on **1a** as well as on **2a** under the standard reaction conditions in the presence of anhydrous dioxane/AcOH/$H_2{}^{18}O$. The HRMS analysis revealed that the formation of both **2a**–^{16}O/**2a**–^{18}O products in both experiments, presumable due to oxygen exchange between $H_2{}^{18}O$ and acetic acid or product **2a**, which is confirmed with HRMS analysis. Notably, these reactions indicates that the oxygen atom originates from two ways such as oxygen exchange with acetic acid and with product **2a**.

IIID. Synthetic utility and control experiments



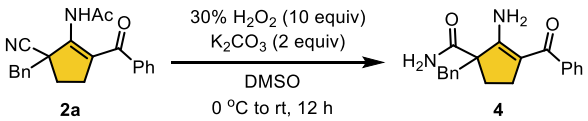
Gram-scale reaction: An oven dried pressure tube was charged with alkyne-tethered malononitrile **1a** (1.0 g, 3.5 mmol), $Pd(OAc)_2$ (39 mg, 5 mol%, 0.18 mmol) and bipyridine (33 mg, 6 mol%, 0.21 mmol) in AcOH:1,4-dioxane (1:4 ratio, 10 mL) under N_2 atmosphere at rt. The reaction mixture was stirred at 80 ^oC in an oil bath for 12 hours (monitored by TLC). Then, it was cooled to room temperature and quenched with aqueous $NaHCO_3$ (40 mL) solution. The mixture was extracted with EtOAc (3 x 40 mL) and concentrated under reduced pressure. The residue was directly subjected to flash column chromatography on silica gel (20% EtOAc/hexanes; R_f = 0.4) to afford the desired product **2a** in 77% yield (0.93 g).

2-Amino-3-benzoyl-1-benzyl cyclopent-2-ene-1-carbonitrile (3):[10]



To compound **2a** (50 mg, 0.15 mmol) a solution of K_2CO_3 (29 mg, 0.22 mmol, 1.5 equiv.) in 2 mL of MeOH was added and the mixture was stirred at rt for 3 h. Then the reaction mixture was filtered through a celite, concentrated and purify by column chromatography (30% EtOAc/hexanes; R_f = 0.3) to obtain enamine **3** as a brownish semisolid (39 mg, 88% yield); ^1H NMR (400 MHz, $CDCl_3$) δ 7.59 – 7.54 (m, 2H), 7.46 – 7.38 (m, 3H), 7.33 (dd, *J* = 7.5, 3.2 Hz, 5H), 3.18 (d, *J* = 13.5 Hz, 1H), 3.09 (d, *J* = 13.5 Hz, 1H), 2.71 – 2.58 (m, 2H), 2.26 (dt, *J* = 12.9, 8.4 Hz, 1H), 2.17 (ddd, *J* = 12.8, 6.0, 3.8 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.5, 161.3, 141.0, 134.2, 130.7, 130.4, 128.8, 128.2, 128.1, 127.4, 120.8, 105.2, 49.9, 42.2, 34.4, 29.1; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{20}H_{19}N_2O^+$ 303.1492; Found 303.1494.

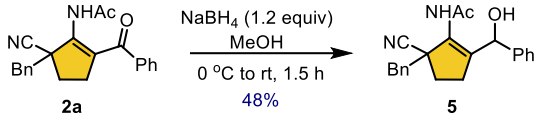
2-Amino-3-benzoyl-1-benzylcyclopent-2-ene-1-carboxamide (4):[11]



To a stirred solution of enamide **2a** (50 mg, 0.15 mmol) in DMSO (2 mL) was added K_2CO_3 (40 mg, 0.29 mmol, 2 equiv.) and 30% aq H_2O_2 (113 µL, 1.5 mmol, 10 equiv.) at 0 °C and stirred at rt

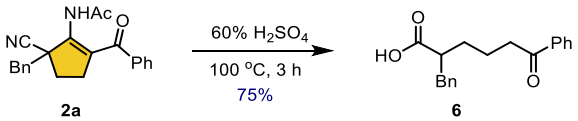
for 12 h. Diluted with excess water (8 mL) and stirred for 12 h. The resulting solid was collected by filtration, washed with water, pet. ether and dried to get 44 mg (94%) of pdt **4** as a white solid. mp = 156-158 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55 (d, *J* = 6.4 Hz, 2H), 7.39 (t, *J* = 6.9 Hz, 3H), 7.27 (dt, *J* = 12.0, 7.0 Hz, 7H), 5.46 (d, *J* = 33.3 Hz, 2H), 3.27 (d, *J* = 13.4 Hz, 1H), 3.07 (d, *J* = 13.3 Hz, 1H), 2.60 – 2.50 (m, 2H), 2.10 – 2.00 (m, 1H), 1.96 – 1.85 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.6, 176.1, 167.0, 141.8, 136.3, 130.4, 130.1, 128.5, 128.1, 127.3, 127.3, 104.0, 59.1, 42.8, 31.1, 28.2; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{20}H_{21}N_2O_2^+$ 321.1598; Found 321.1600.

***N*-(5-Benzyl-5-cyano-2-(hydroxy(phenyl)methyl)cyclopent-1-en-1-yl)acetamide (5):**[12]



In an oven-dried 10 mL round-bottom flask was charged with enamide **2a** (60 mg, 0.17 mmol) and added 2.0 mL of absolute methanol under nitrogen atmosphere, and the resulting solution was cooled to 0 °C. Later $NaBH_4$ (8 mg, 0.21 mmol, 1.2 eq) was added to the reaction mixture in one portion and the resulting mixture was stirred at 0 °C to rt. After 1.5 h, the reaction mixture was quenched with 2 mL of saturated NH_4Cl solution diluted with 5 mL CH_2Cl_2 and extracted with additional CH_2Cl_2 (2 × 5 mL). Combined organic solvent was dried over anhydrous Na_2SO_4 and concentrated in *vacuo*. The crude reaction mixture was purified by silica gel flash column chromatography (30% EtOAc/hexanes; R_f = 0.5) to obtain alcohol **5** as a yellowish orange semisolid (29 mg, 48% yield); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 – 7.51 (m, 10H), 5.69 (s, 1H), 4.62 (s, 1H), 3.33 (d, *J* = 13.7 Hz, 1H), 3.17 (d, *J* = 13.7 Hz, 1H), 2.72 – 2.62 (m, 1H), 2.44 (ddd, *J* = 10.9, 8.2, 2.8 Hz, 1H), 2.40 – 2.35 (m, 1H), 2.33 (s, 3H), 2.31 – 2.23 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.7, 140.6, 140.6, 135.2, 129.9, 129.0, 128.8, 128.4, 128.0, 127.4, 125.7, 121.6, 69.0, 50.7, 43.1, 34.1, 27.8, 23.3; HRMS (ESI) m/z: $[M+H-H_2O]^+$ Calcd for $C_{22}H_{21}N_2O^+$ 333.1654; Found 329.1638.

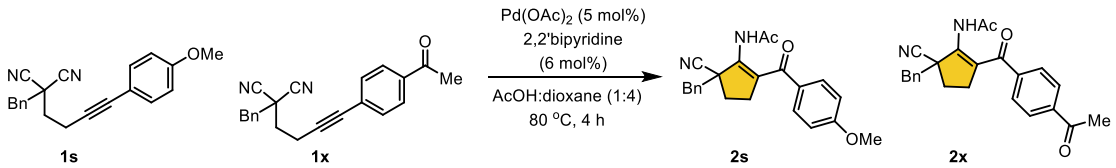
2-Benzyl-6-oxo-6-phenylhexanoic acid (6):[13]



In an oven-dried 10 mL round-bottom flask was charged with enamide **2a** (30 mg, 0.1 mmol) and added 0.2 mL of H_2SO_4 then the resulting solution was heated at 100 °C for 3 h. Reduced to room temperature, diluted with 5mL of water, extracted three times with 8mL of dichloromethane,

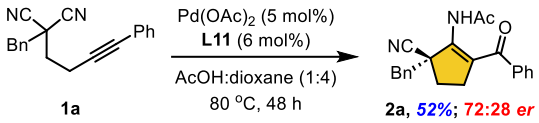
combined with the dichloromethane phase, and dried over anhydrous Na_2SO_4 and concentrated in *vacuo*. The crude reaction mixture was purified by silica gel flash column chromatography (30% EtOAc/hexanes; R_f = 0.3) to obtain alcohol **6** as a colorless solid (19 mg, 75% yield); mp = 83-85 ^oC; ^1H NMR (400 MHz, $CDCl_3$) δ 7.95 (dd, *J* = 5.2, 3.3 Hz, 2H), 7.58 (tt, *J* = 7.4, 1.9 Hz, 1H), 7.47 (dd, *J* = 10.4, 4.7 Hz, 2H), 7.35 – 7.27 (m, 2H), 7.22 (ddd, *J* = 8.3, 5.9, 3.0 Hz, 3H), 3.01 (ddd, *J* = 13.8, 9.2, 5.0 Hz, 3H), 2.87 – 2.71 (m, 2H), 1.92 – 1.72 (m, 3H), 1.71 – 1.59 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.9, 181.0, 139.0, 137.0, 133.2, 129.0, 128.7, 128.6, 128.2, 126.6, 47.3, 38.3, 38.2, 31.3, 22.0; HRMS (ESI) m/z: $[M-H]^+$ Calcd for $C_{19}H_{19}O_3^+$ 295.1329; Found 295.1330.

Intermolecular competition experiment:



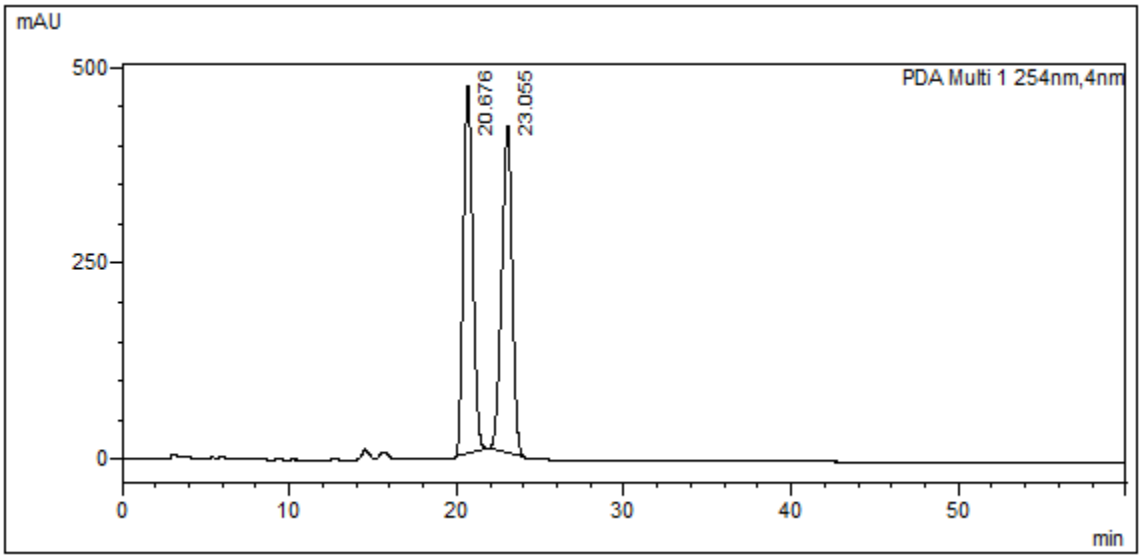
A dried screw-cap vial was charged with alkyne-tethered malononitrile **1s** (30 mg, 0.1 mmol), **1x** (30 mg, 0.1 mmol), $Pd(OAc)_2$ (1.2 mg, 0.005 mmol, 5 mol%), and bipyridine (1 mg, 0.006 mmol, 6 mol%) in AcOH:1,4 dioxane (1:4 ratio, 0.1+0.4 mL) under N_2 atmosphere at rt. The reaction mixture was stirred at 80 ^oC in an oil bath for 4 hours. Then, it was cooled to room temperature and quenched with aqueous $NaHCO_3$ (8 mL) solution. The mixture was extracted with EtOAc (3x8 mL) and concentrated under reduced pressure. The residue was directly subjected to flash column chromatography on silica gel to afford desired products **2s** and **2x** in a 1.8:1 ratio, with 27% and 15% yields respectively.

IIIE. Asymmetric cyclization of alkyne-tethered malononitrile



A dried screw-cap vial was charged with a magnetic stirring bar, $Pd(OAc)_2$ (1.2 mg, 5 mol%, 0.005 mmol), and **L11** (1.3 mg, 6 mol%) were dissolved in 1,4 dioxane (0.4 mL) and stirred for 15 min at room temperature under nitrogen atmosphere. Later, alkyne-tethered malononitrile **1a** (0.1 mmol, 1 equiv) and acetic acid (0.1 mL) were added at the same temperature. The resulting mixture

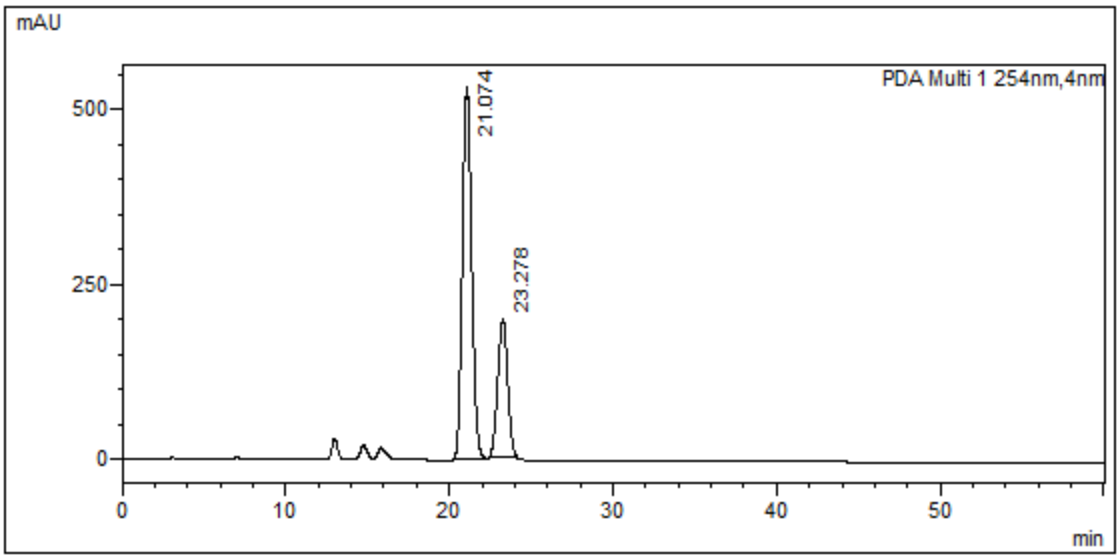
was stirred at 80 °C using preheated oil bath for 48 hours (monitored by TLC). After, it was cooled to room temperature and quenched with aqueous $NaHCO_3$ (8 mL) solution. The mixture was extracted with EtOAc (3 x 8 mL) and concentrated under reduced pressure. The residue was directly subjected to flash column chromatography on silica gel to afford the desired product **2a** in 52% yield with 72:28 *er*. $[\alpha]^{20}$ D = +17.33° (c 1.2, $CHCl_3$); Chiral HPLC analysis of the product: Daicel Chiralpak AD-H 250X4.6 mm 5µ column; hexane/2-propanol = 90/10, detected at 254 nm, Flow rate = 1 mL/min, Retention times: 21.074 min (major), 23.278 min (minor).



<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Area%	Height%
1	20.676	18275582	468601	50.252	52.909
2	23.055	18091975	417070	49.748	47.091
Total		36367557	885670	100.000	100.000



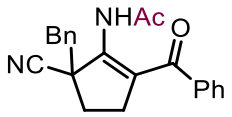
<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Area%	Height%
1	21.074	21131885	532631	71.721	72.891
2	23.278	8332299	198087	28.279	27.109
Total		29464184	730718	100.000	100.000

IV. Single crystal X-ray analysis:

IVa. X-ray crystallographic data for compound 2a:



2a; CCDC 2395429

The purified compound **2a** was dissolved in a mixed solvent of CH_2Cl_2/*n*-hexane (1:9), and placed in a dark cabinet for slow evaporation. Colorless crystals were collected after few days for X-ray analysis.

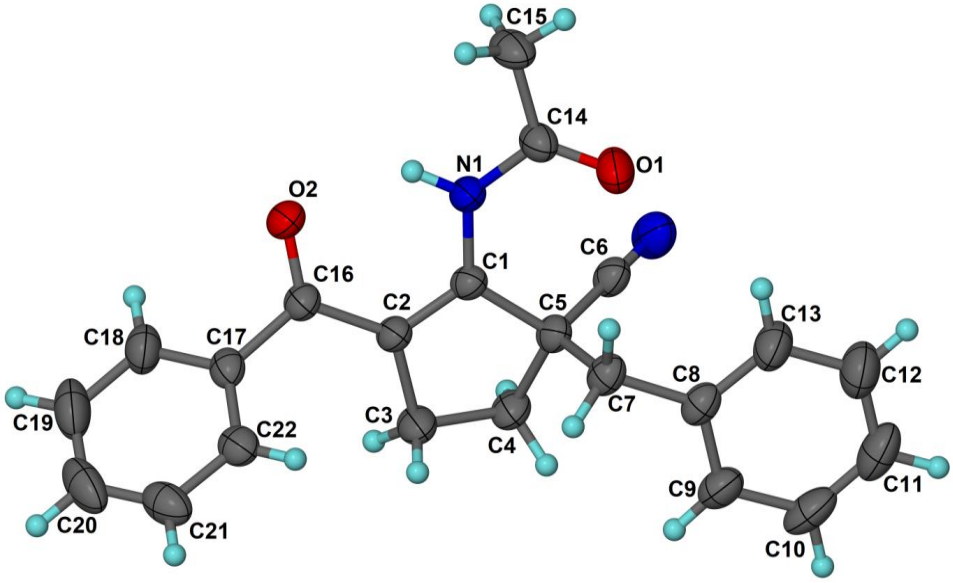


Figure caption: ORTEP diagram of compound **2a** (KB845) compound with the atom-numbering. Displacement ellipsoids are drawn at the 35% probability level and H atoms are shown as small spheres of arbitrary radius.

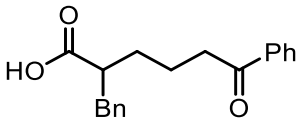
Crystal data for Compound 2a (KB845): $C_{22}H_{20}N_2O_2$, M = 344.40, Monoclinic, Space group *Cc* (No.9), a = 12.1282(11)Å, b = 20.2533(17)Å, c = 7.5226(6)Å, α = 90°, β = 91.106(4)°, γ = 90°, V = 1847.5(3)Å^3, Z = 4, D_c = 1.238 g/cm^3, F_{000} = 728, Bruker D8 QUEST PHOTON III C7 HPAD detector, Mo-Kα radiation, λ = 0.71073 Å, T = 294(2)K, $2\theta_{max}$ = 56º, μ = 0.080 mm^{-1}, 17414 reflections collected, 4227 unique (R_{int} = 0.0410), 240 parameters, *R1* = 0.0392, *wR2* = 0.0903, *R* indices based on 2764 reflections with I > 2σ(I) (refinement on F^2), Final *GooF* = 0.998, largest difference hole and peak = -0.113 and 0.092 e.Å^{-3}. The **CCDC deposition number 2395429** contains the supplementary crystallographic data for this paper which can be obtained free of charge at https://www.ccdc.cam.ac.uk/structures/

Data collection and Structure solution details:

X-ray data for the compound were collected at room temperature on a Bruker D8 QUEST instrument with an IμS Mo microsource (λ = 0.7107 Å) and a PHOTON-III C7 HPAD detector. The raw data frames were reduced and corrected for absorption effects using the Bruker Apex 3 software suite programs[14]. The structure was solved using intrinsic phasing method[15] and further refined with the SHELXL[15-17] program and expanded using Fourier techniques. Anisotropic

displacement parameters were included for all non-hydrogen atoms. All C bound H atoms were positioned geometrically and treated as riding on their parent C atoms [C-H = 0.93-0.97 Å, and Uiso(H) = 1.5Ueq(C) for methyl H or 1.2Ueq(C) for other H atoms]. The N bound protons were located in the difference Fourier map and their positional coordinates were allowed to refine. **CCDC deposition number 2395429** contains the supplementary crystallographic data for this paper which can be obtained free of charge at https://www.ccdc.cam.ac.uk/structures/

IVb. X-ray crystallographic data for compound 6:



2a; **CCDC 2396659**

The purified compound **6** was dissolved in a mixed solvent of CH_2Cl_2/*n*-hexane (1:9), and placed in a dark cabinet for slow evaporation. Colorless crystals were collected after few days for X-ray analysis.

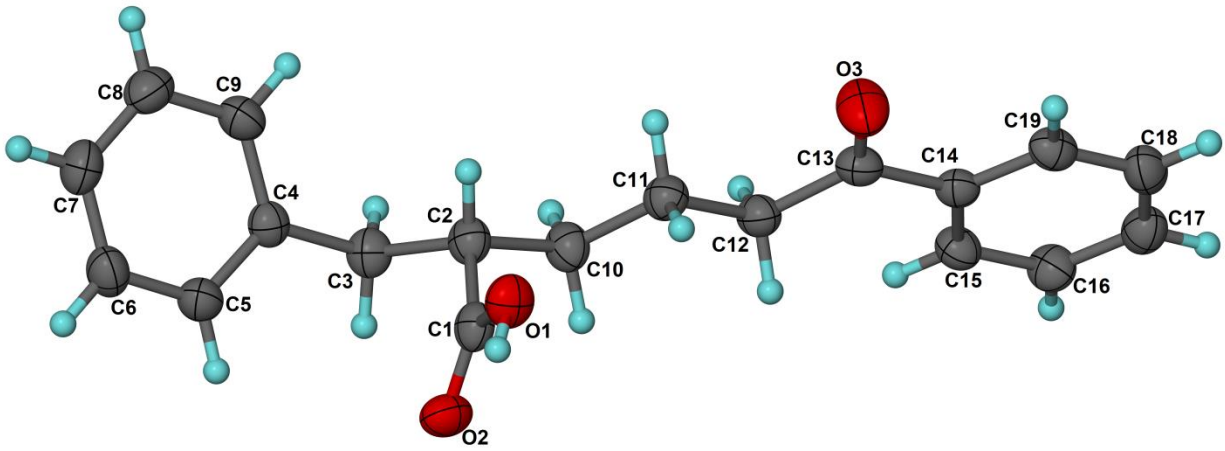


Figure caption: ORTEP diagram of compound **6** (KB1655) compound with the atom-numbering. Displacement ellipsoids are drawn at the 35% probability level and H atoms are shown as small spheres of arbitrary radius.

Crystal data for compound 6 (KB1655): $C_{19}H_{20}O_3$, M = 296.35, Monoclinic, Space group $P2_1/c$ (No.14), a = 12.6120(14)Å, b = 5.6910(6)Å, c = 22.766(3)Å, α = 90°, β = 103.590(5)°, γ = 90°, V = 1588.2(3)Å^3, Z = 4, D_c = 1.239 g/cm^3, F_{000} = 632, Bruker D8 QUEST PHOTON III C7 HPAD detector, Mo-Kα radiation, λ = 0.71073 Å, T = 294(2)K, $2\theta_{max}$ = 55º, μ = 0.083 mm^{-1}, 26864 reflections collected, 3649 unique (R_{int} = 0.0620), 220 parameters, *R1* = 0.0517, *wR2* = 0.1369, *R* indices based on 2251 reflections with I > 2σ(I) (refinement on F^2), Final *GooF* = 1.042, largest difference hole and peak = -0.144 and 0.213 e.Å^{-3}. The **CCDC deposition number 2396659** contains the supplementary crystallographic data for this paper which can be obtained free of charge at https://www.ccdc.cam.ac.uk/structures/

Data collection and Structure solution details:

X-ray data for the compound were collected at room temperature on a Bruker D8 QUEST instrument with an IμS Mo microsource (λ = 0.7107 Å) and a PHOTON-III C7 HPAD detector. The raw data frames were reduced and corrected for absorption effects using the Bruker Apex 3 software suite programs[14]. The structure was solved using intrinsic phasing method[15] and further refined with the SHELXL[15-17] program and expanded using Fourier techniques. Anisotropic displacement parameters were included for all non-hydrogen atoms. All C bound H atoms were positioned geometrically and treated as riding on their parent C atoms [C-H = 0.93-0.97 Å, and Uiso(H) = 1.5Ueq(C) for methyl H or 1.2Ueq(C) for other H atoms]. The oxygen atoms of the carboxylic acid were disordered over two sites, with site occupancy factor of 0.56(3) for the major component of the disordered atoms (O1/O2) and 0.44(3) for the minor component of the disordered atoms (O1D/O2D). PART, FVAR, DELU, and SIMU instructions were utilized for modelling the structural disorder and structural refinement[17]. **CCDC deposition number 2396659** contains the supplementary crystallographic data for this paper which can be obtained free of charge at https://www.ccdc.cam.ac.uk/structures/

V. References

1. B. Tian, X. Li, P. Chen and G. Liu, *Angew. Chem., Int. Ed.,* 2021, **133**, 15007–15012.
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10. Current Patent Assignee: JANSSEN PHARMACEUTICA - WO2022/63896, 2022, A1 Location in patent: Page/Page column 92-93
11. Current Patent Assignee: ACETYLON PHARMACEUTICALS - US2015/105384, 2015, A1 Location in patent: Paragraph 0331; 0332.
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13. Current Patent Assignee: JIANGSU FLAG CHEM IND - CN114790139, 2022, A Location in patent: Paragraph 0055-0062.
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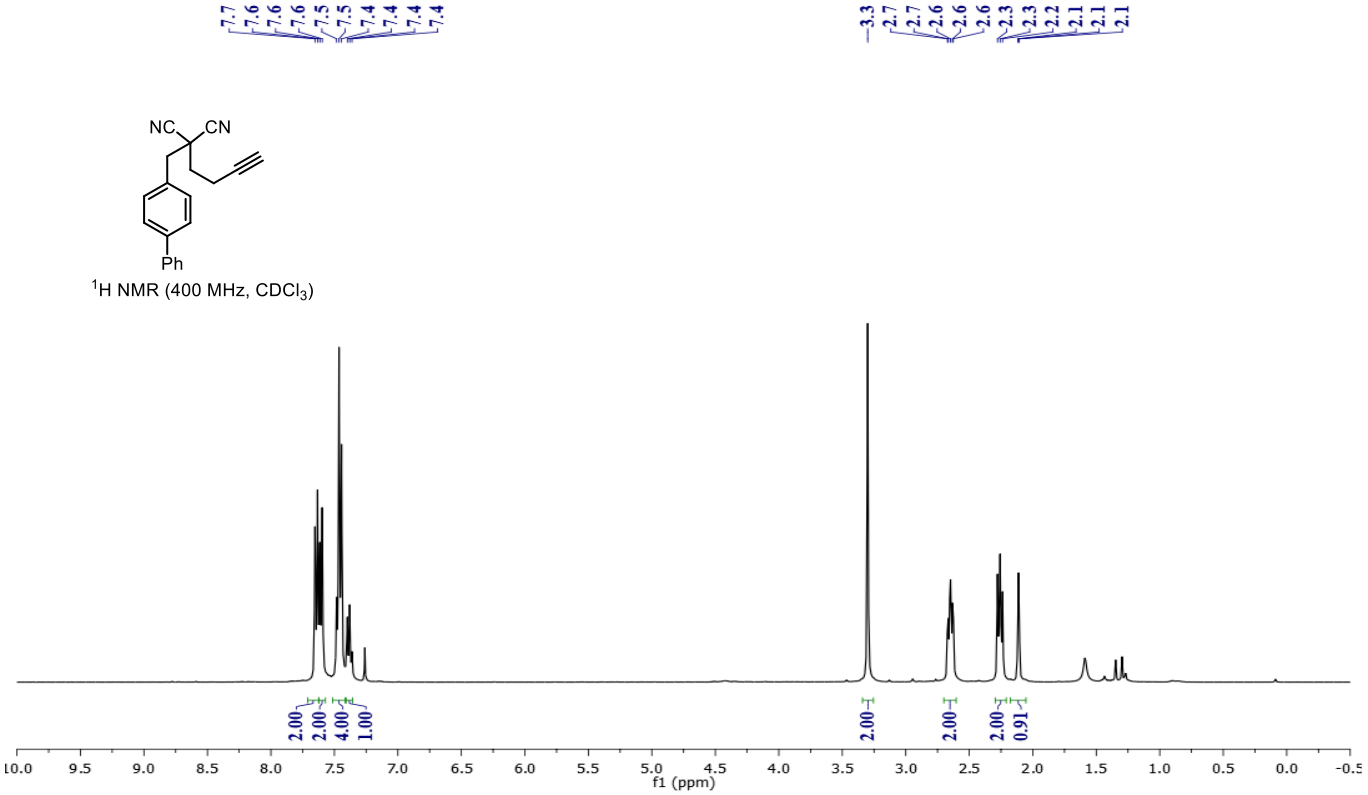
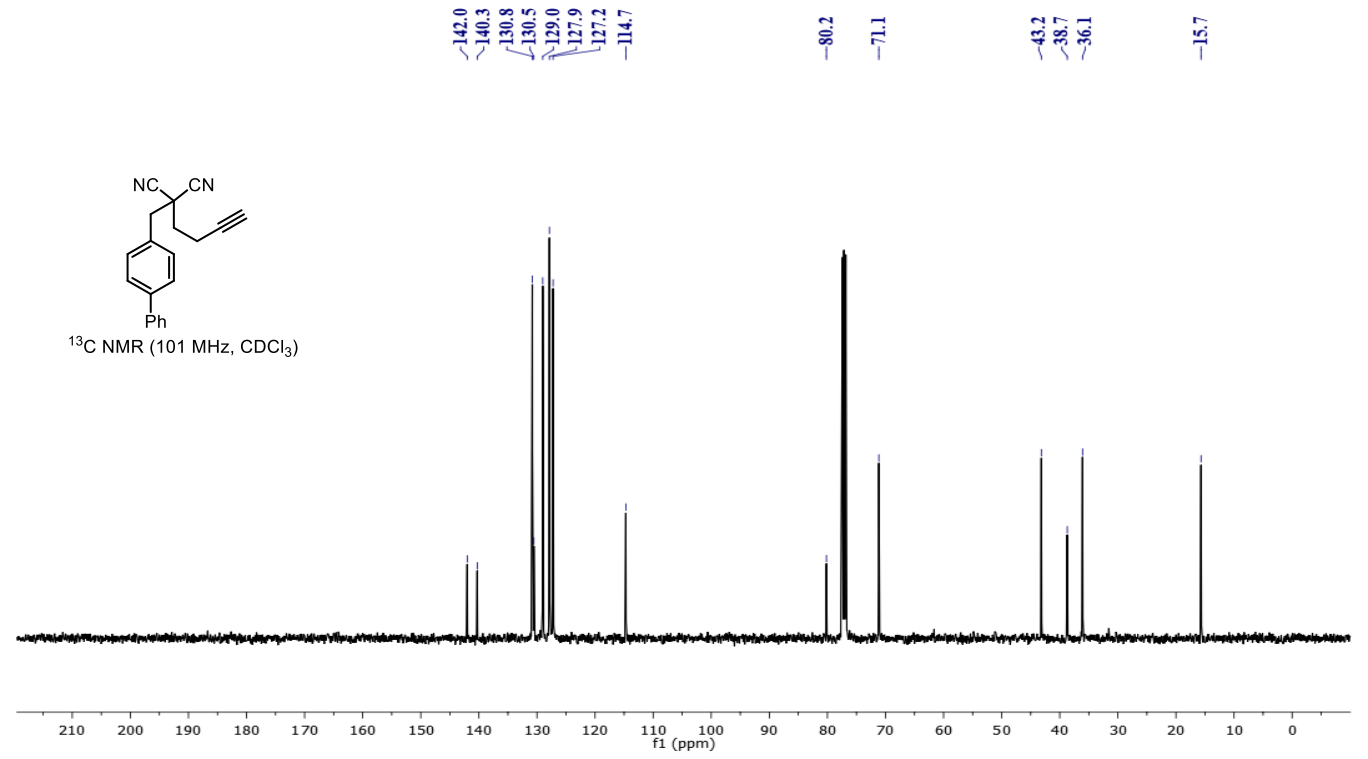
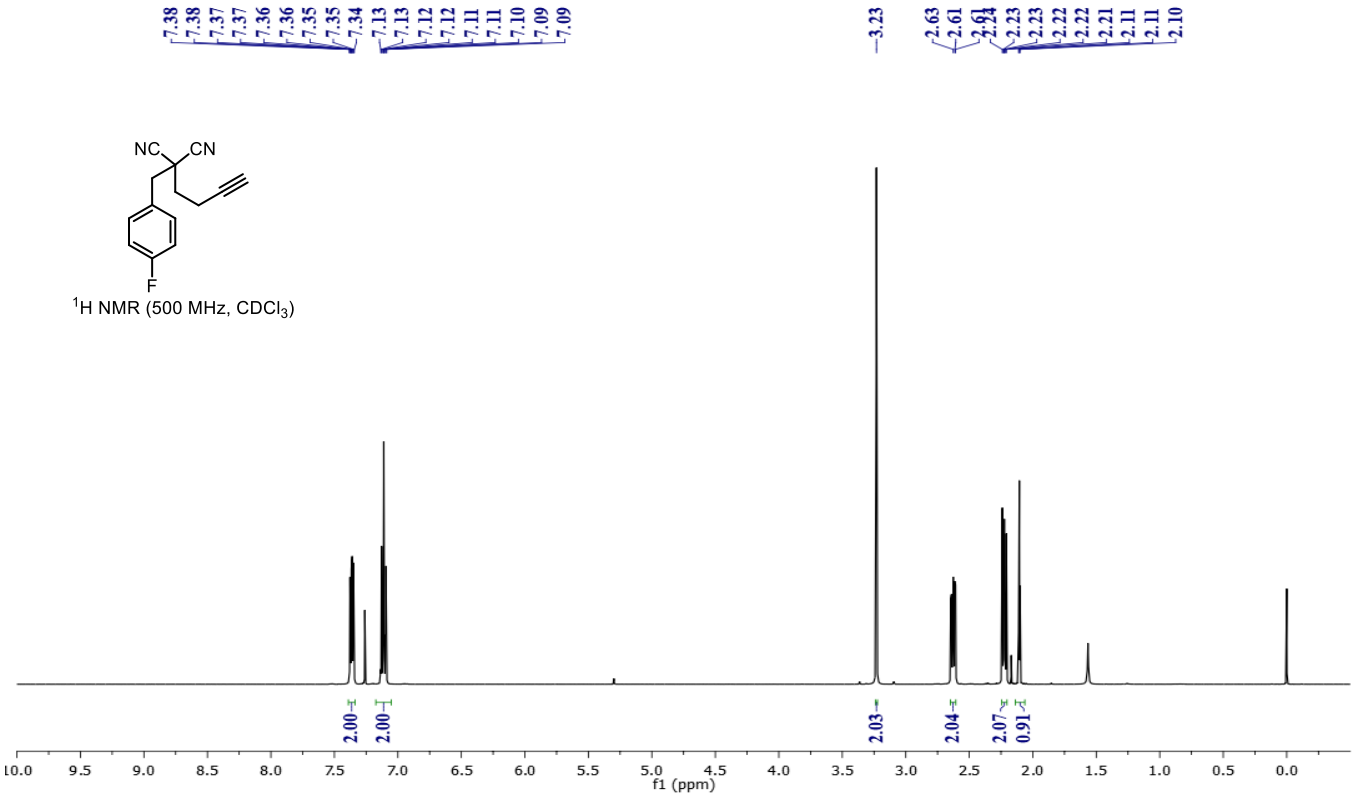
VI. ^{1}H and ^{13}C spectra

2-([1,1'-Biphenyl]-4-ylmethyl)-2-(but-3-yn-1-yl)malononitrile (S9c):

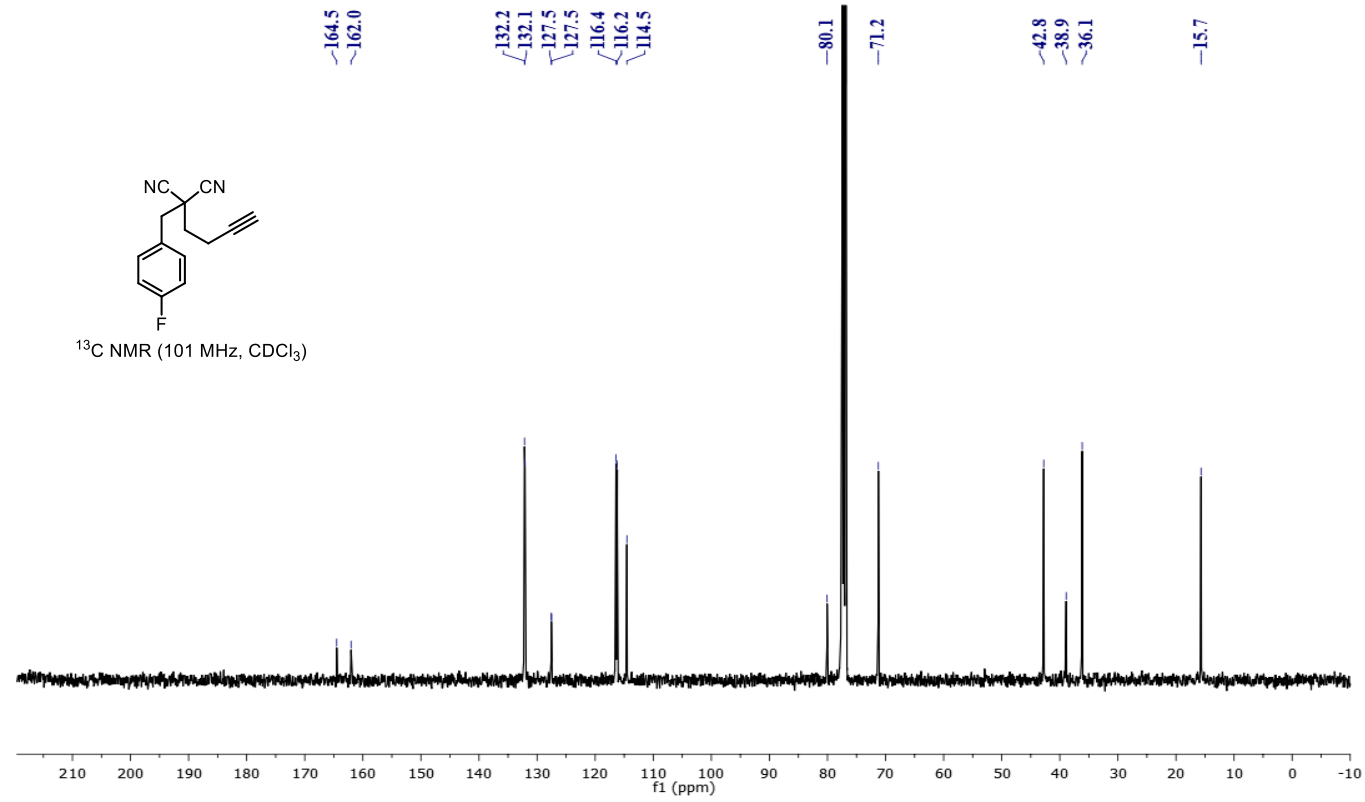




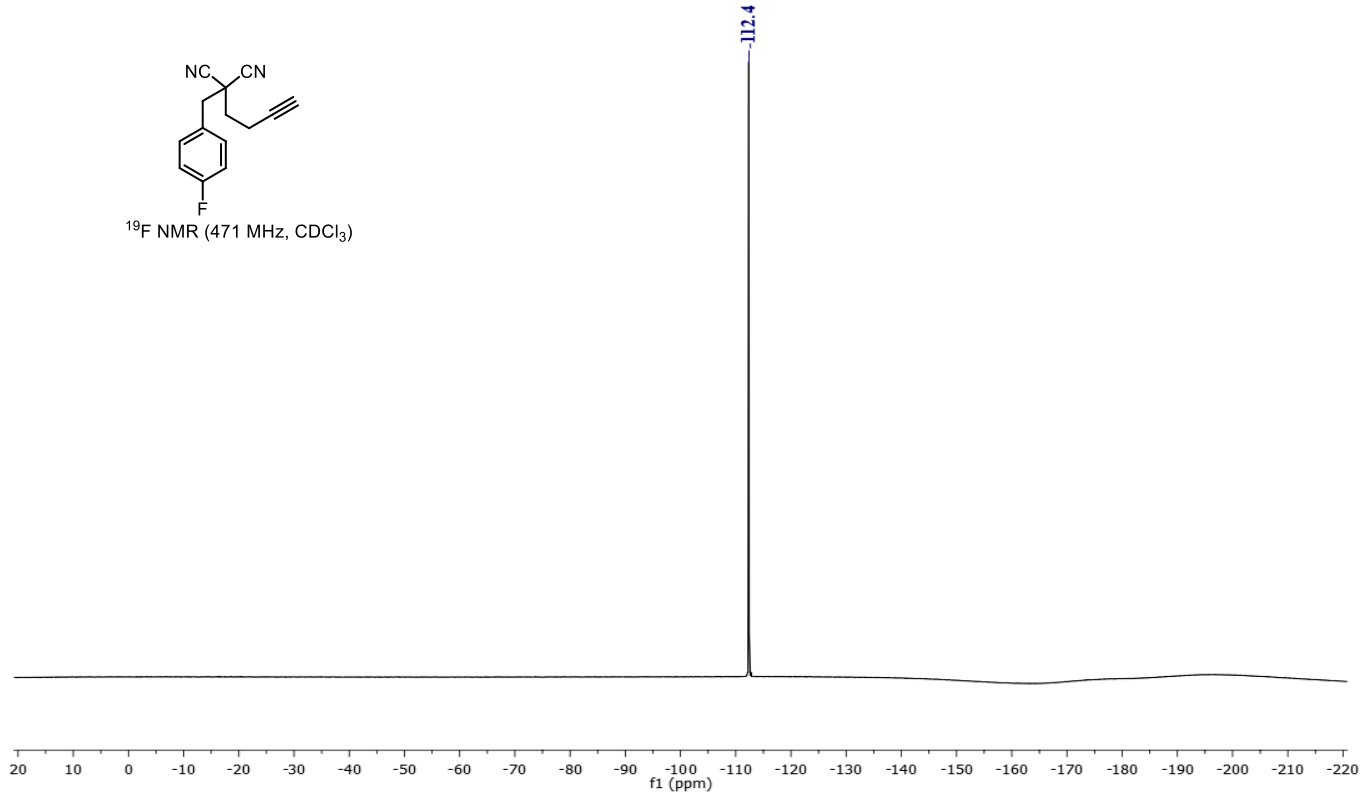
2-(But-3-yn-1-yl)-2-(4-fluorobenzyl)malononitrile (S9d):



^{1}H NMR (500 MHz, $CDCl_3$)

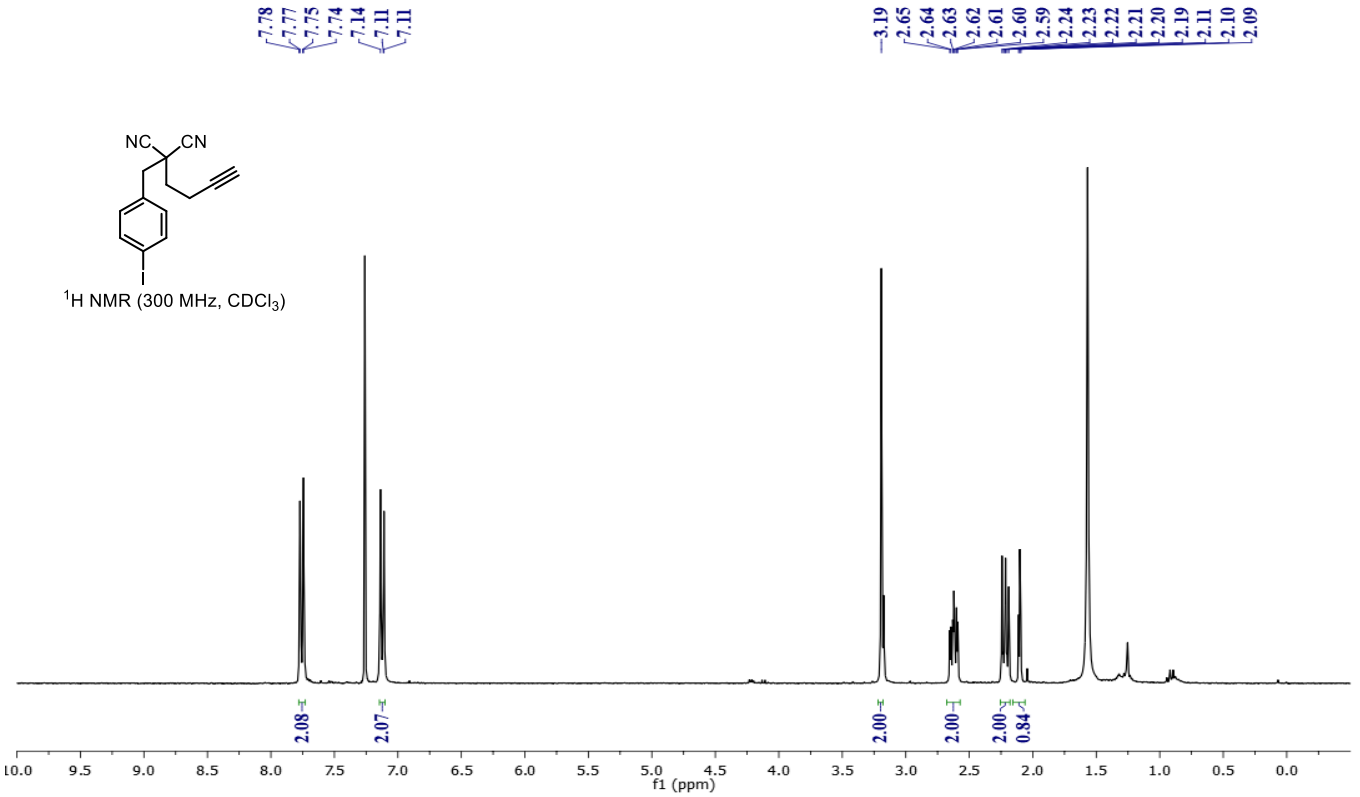


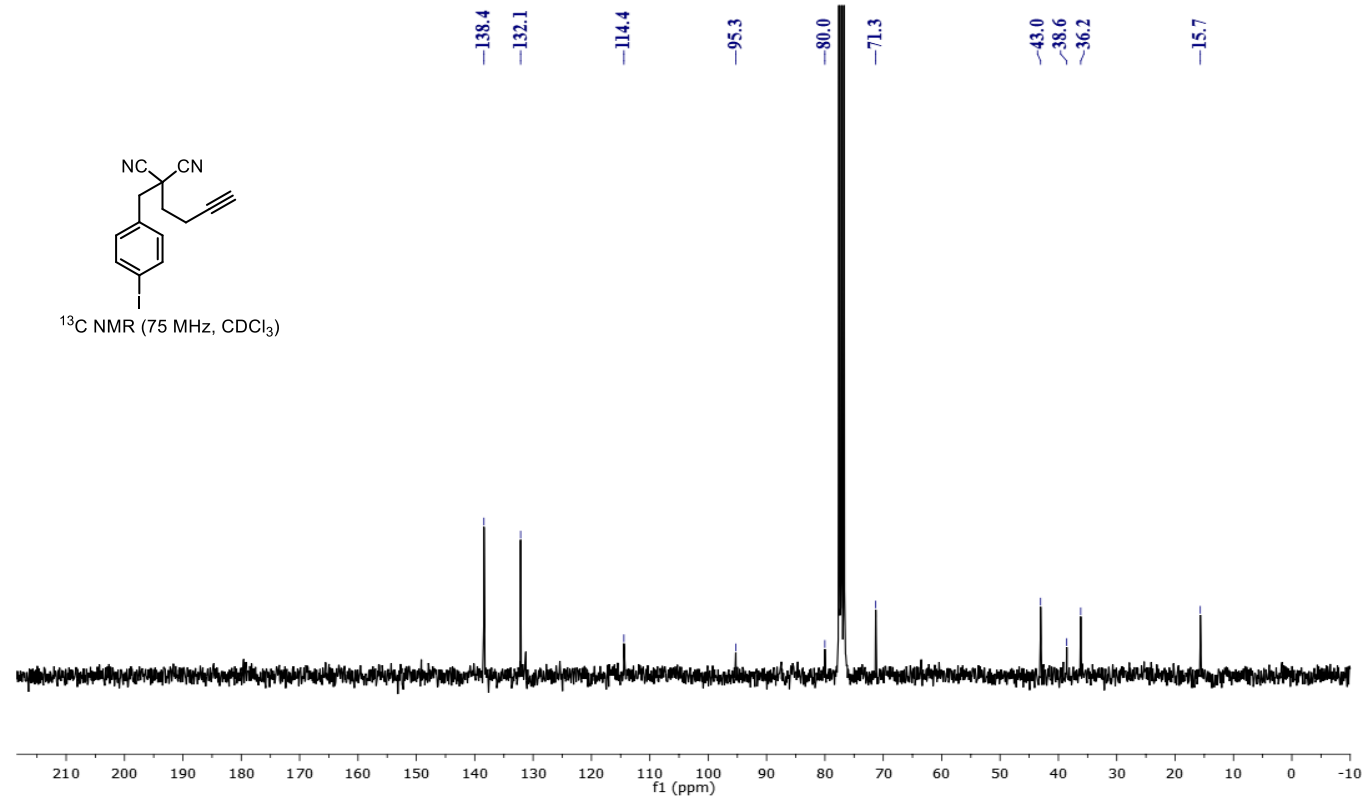
^{13}C NMR (101 MHz, $CDCl_3$)



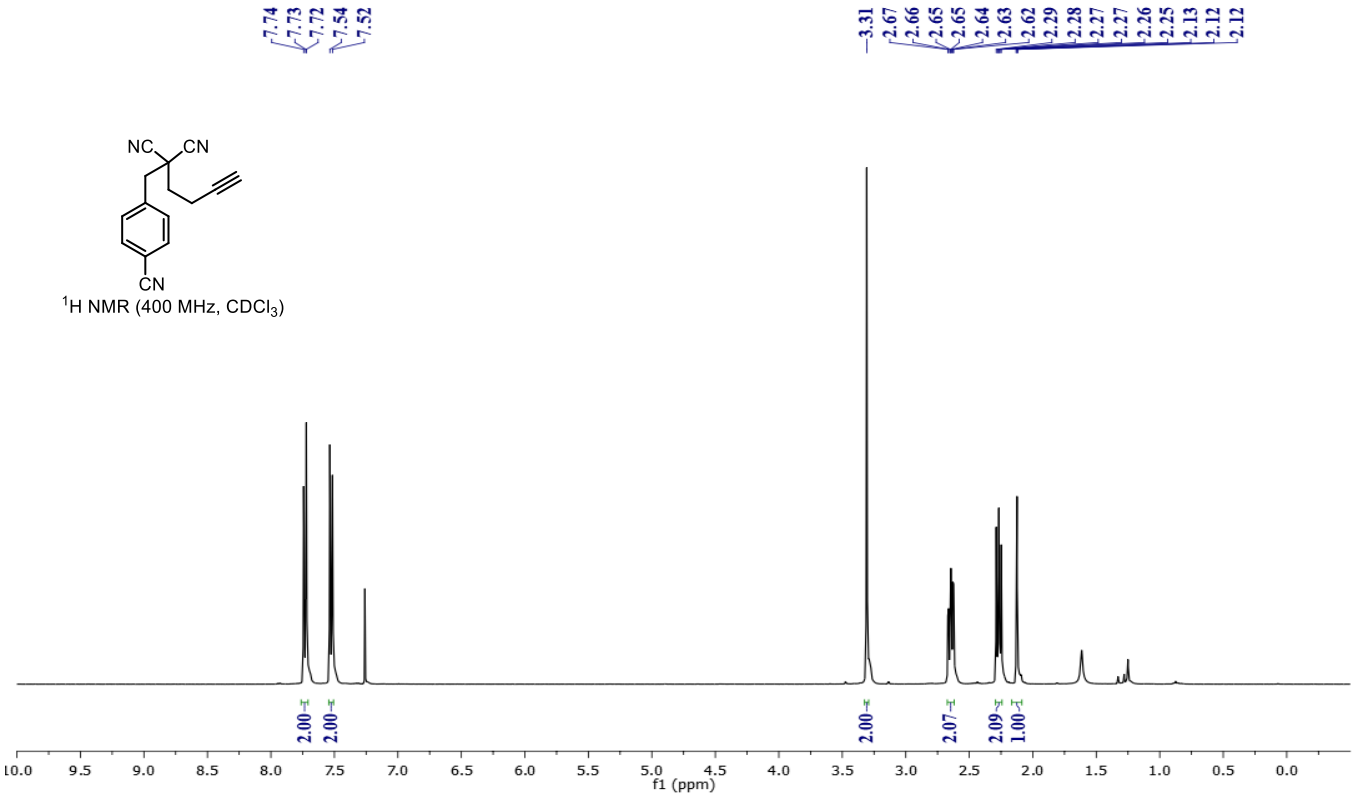
^{19}F NMR (471 MHz, $CDCl_3$)

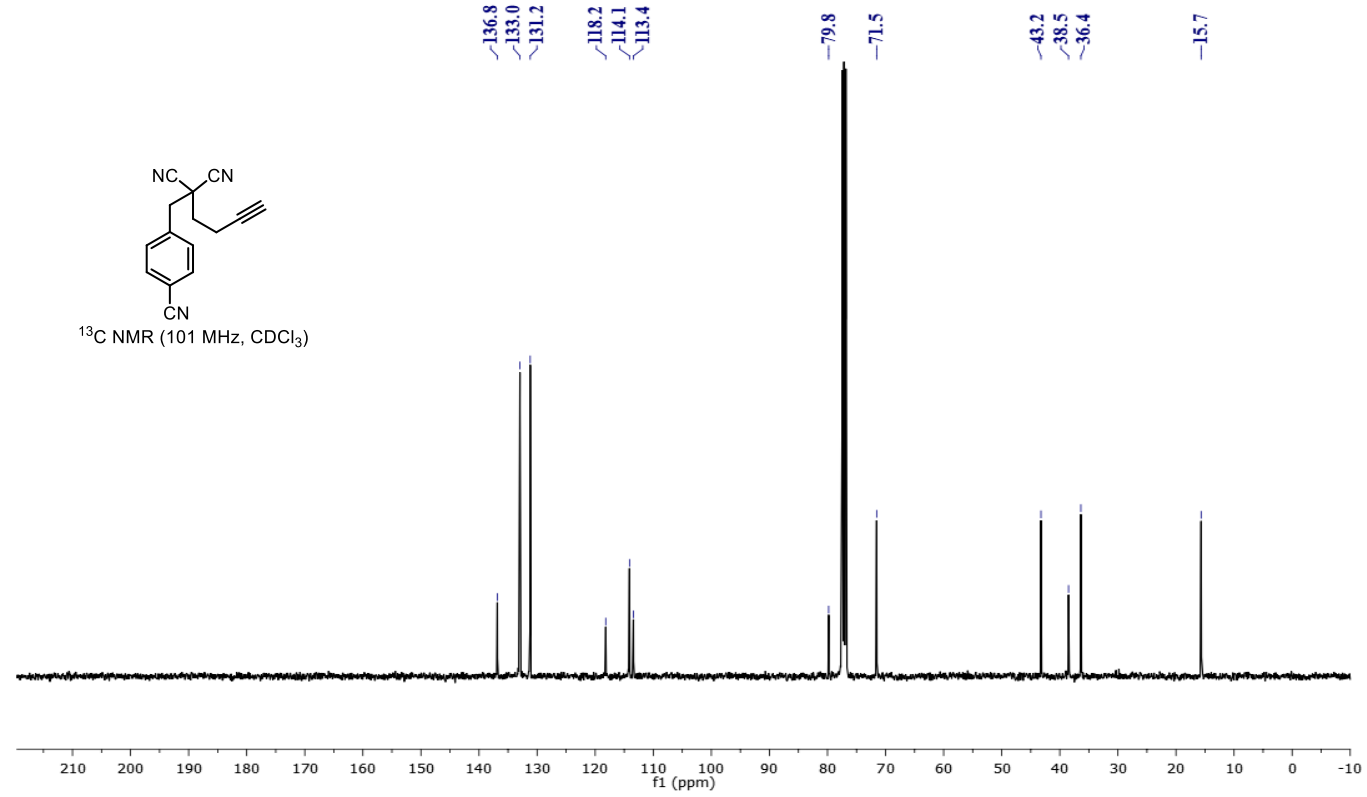
2-(But-3-yn-1-yl)-2-(4-iodobenzyl)malononitrile (S9e):



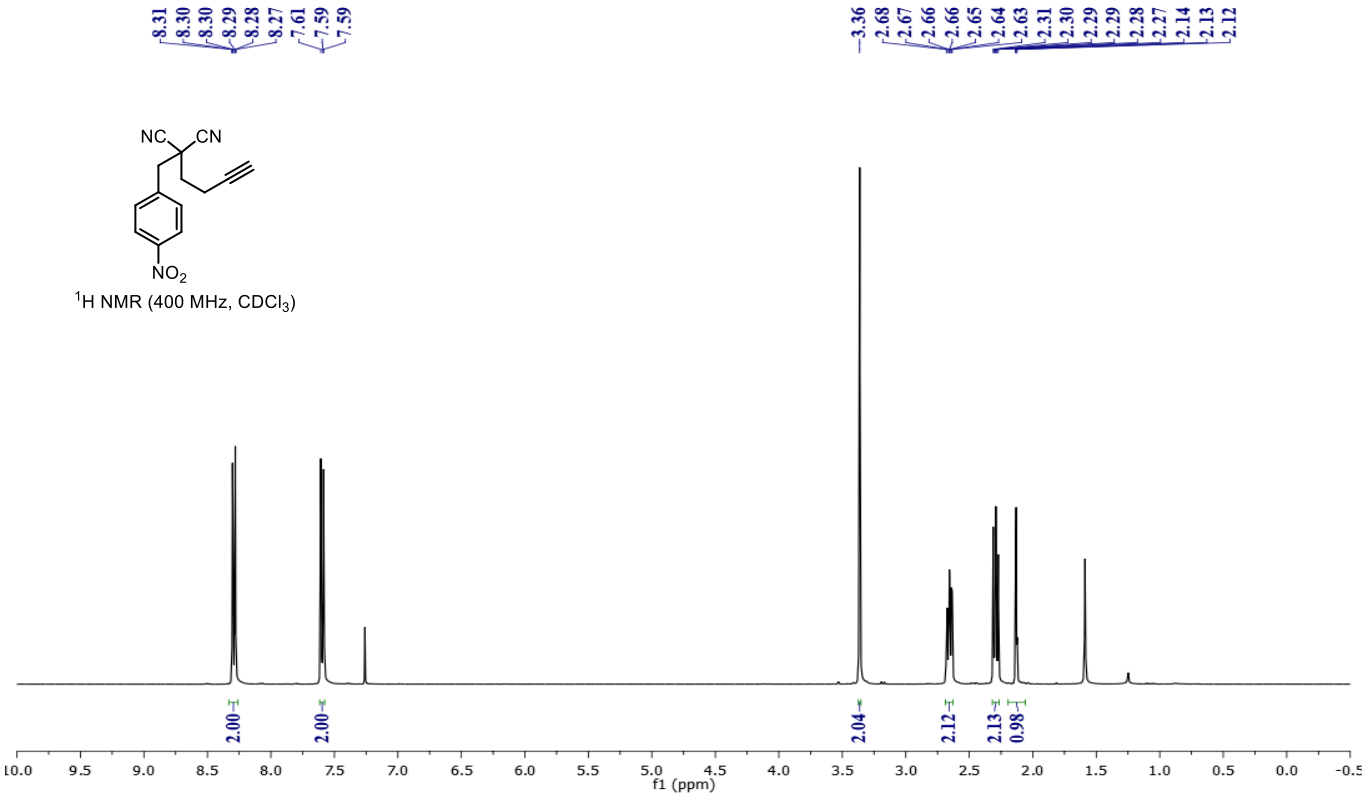


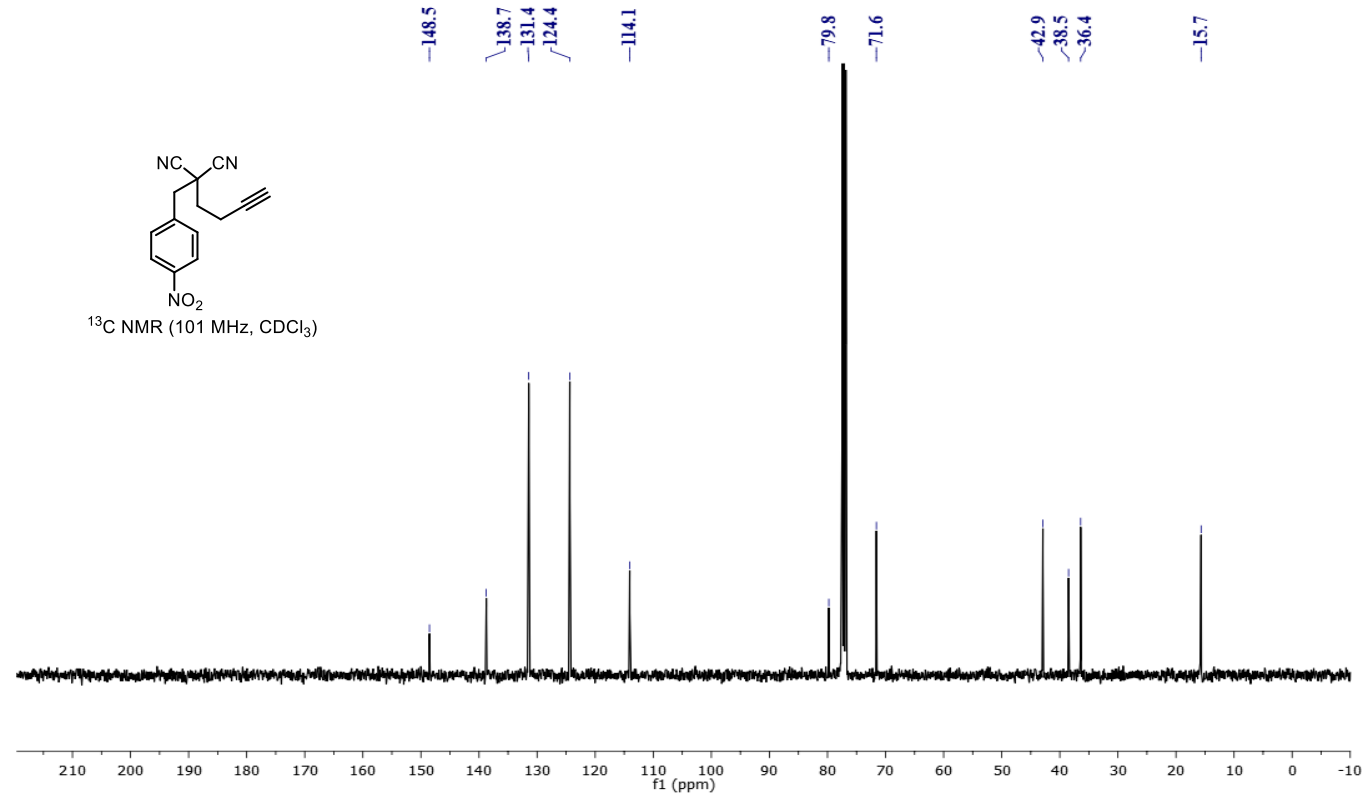
2-But-3-yn-1-yl)-2-(4-cyanobenzyl)malononitrile (S9f):



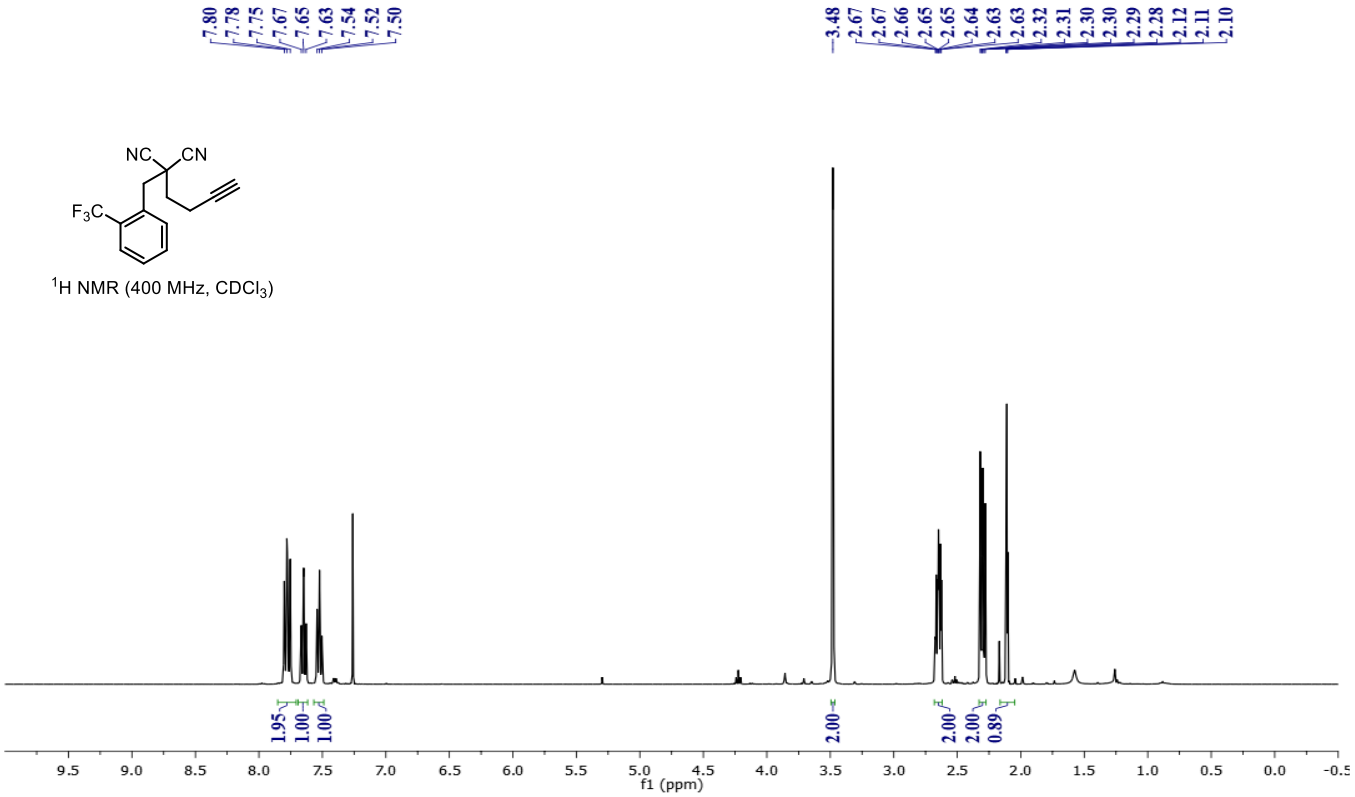


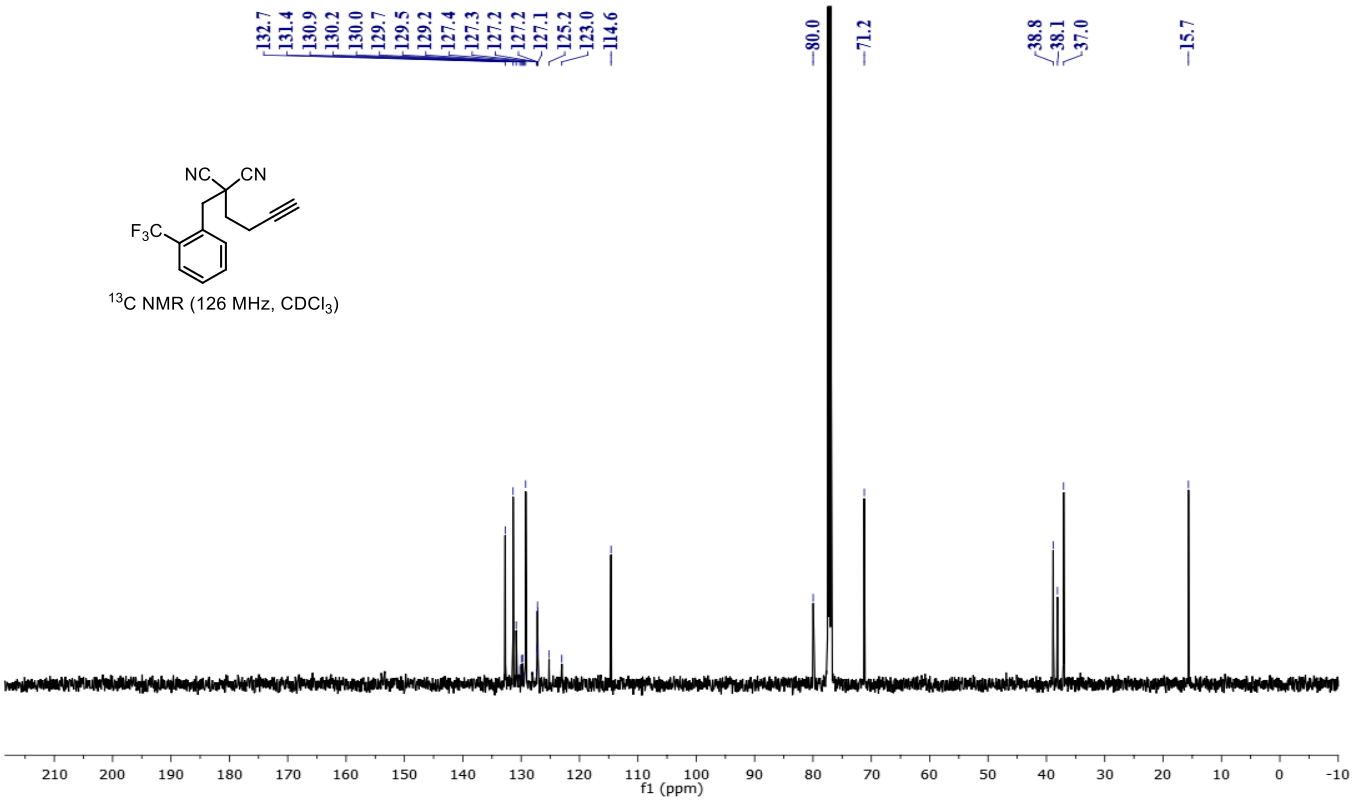
2-(but-3-yn-1-yl)-2-(4-nitrobenzyl)malononitrile (S9g):

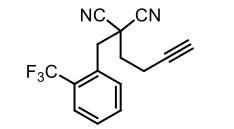




2-(But-3-yn-1-yl)-2-(2-(trifluoromethyl)benzyl)malononitrile (S9h):

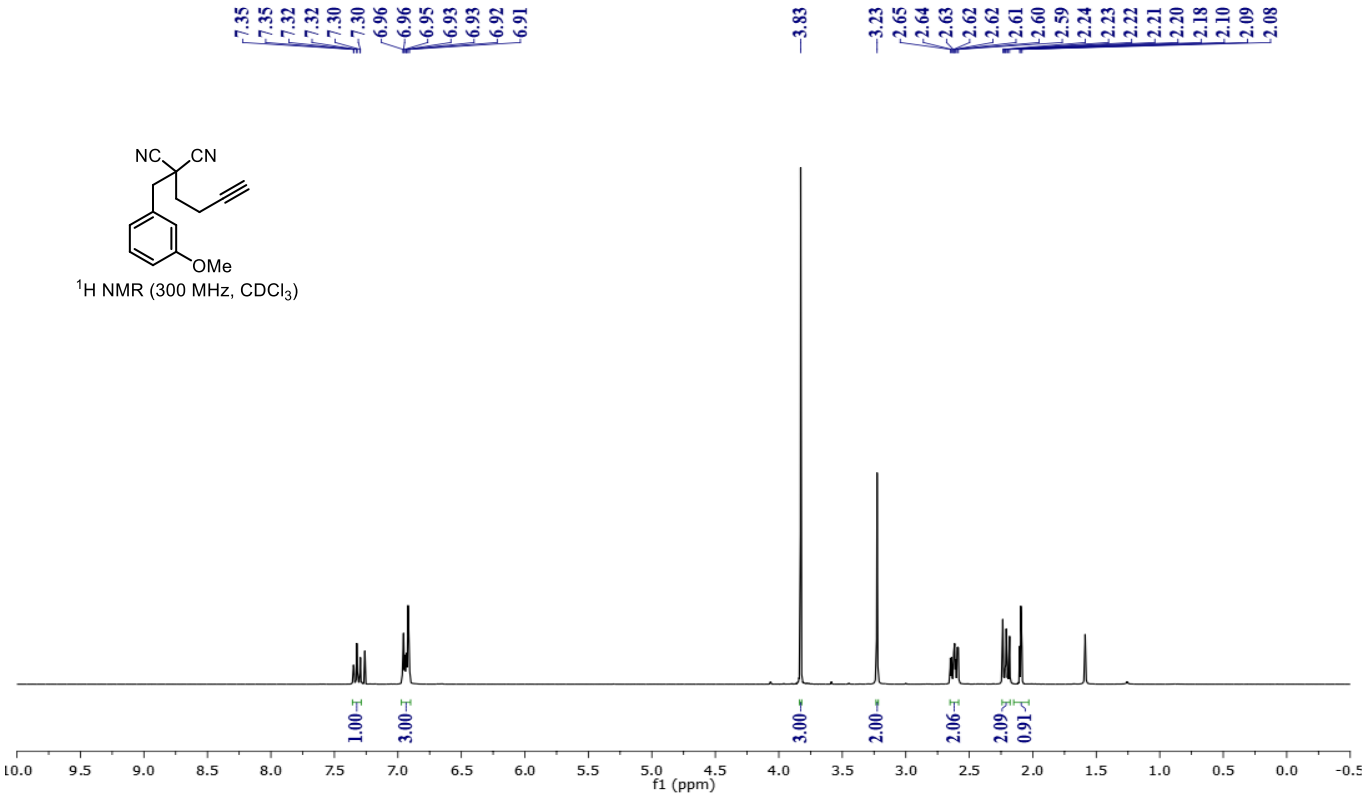




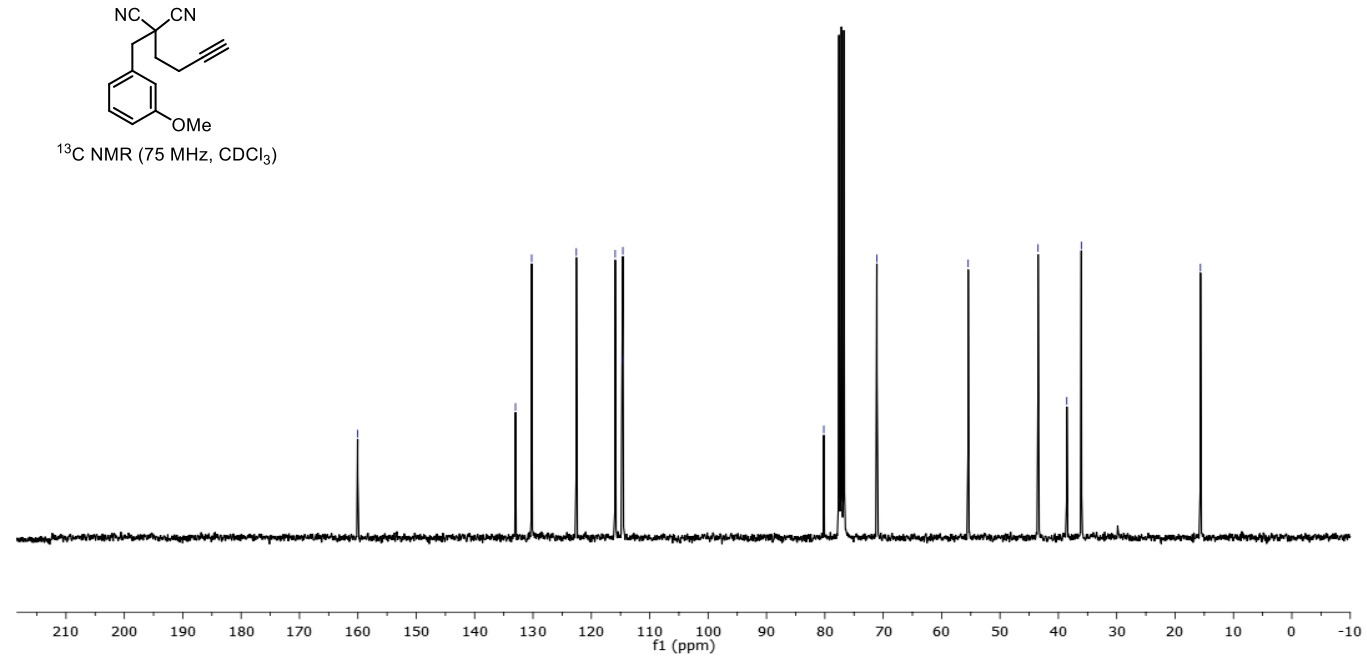


^{19}F NMR (471 MHz, $CDCl_3$)

2-(But-3-yn-1-yl)-2-(3-methoxybenzyl)malononitrile (S9j):

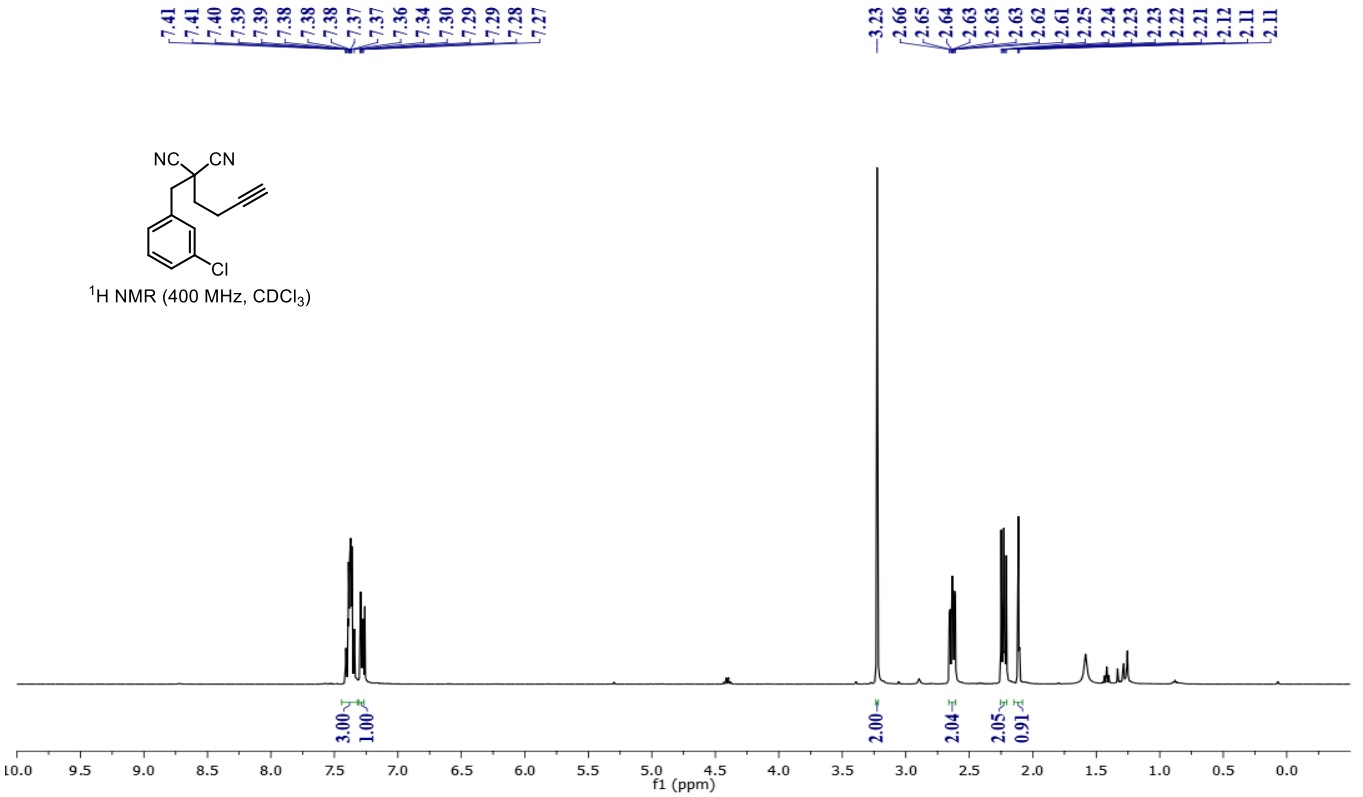


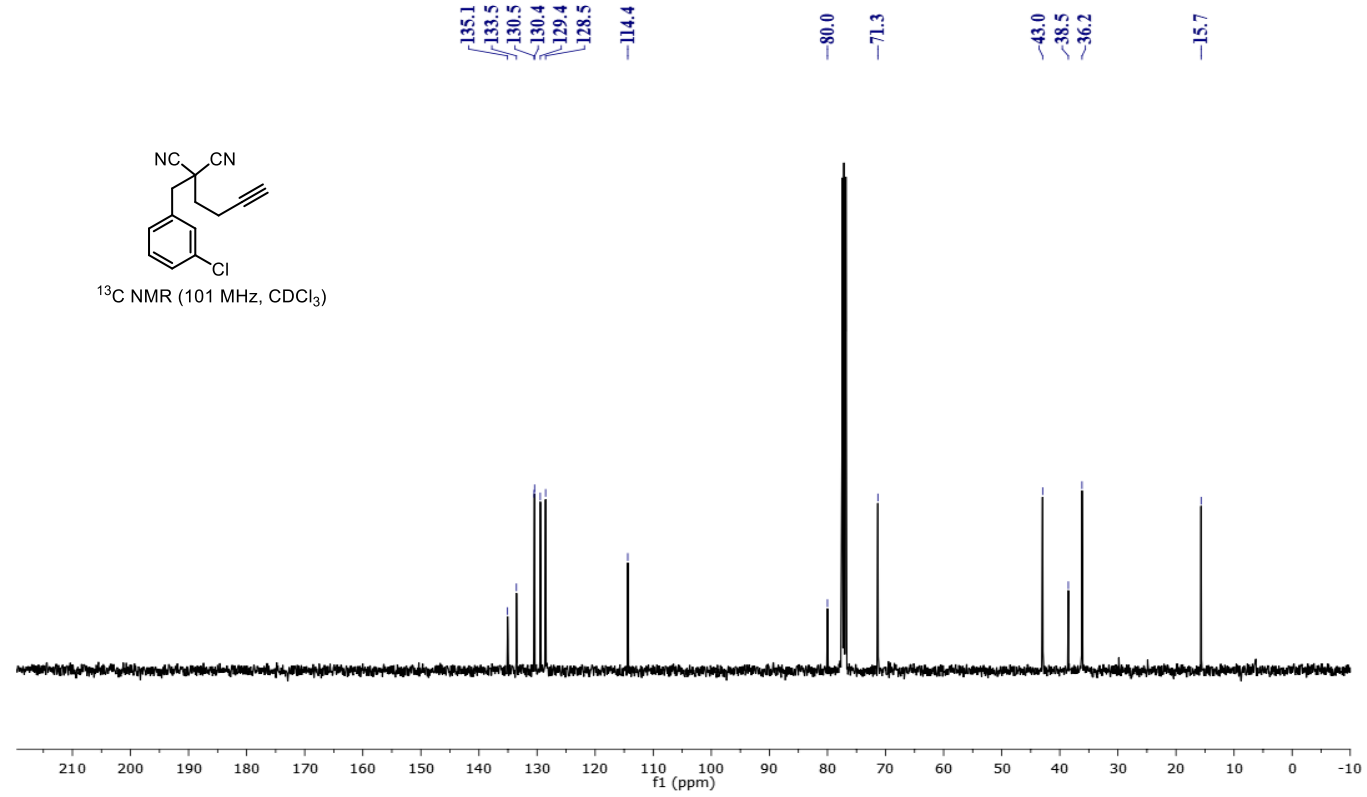
^{1}H NMR (300 MHz, $CDCl_3$)



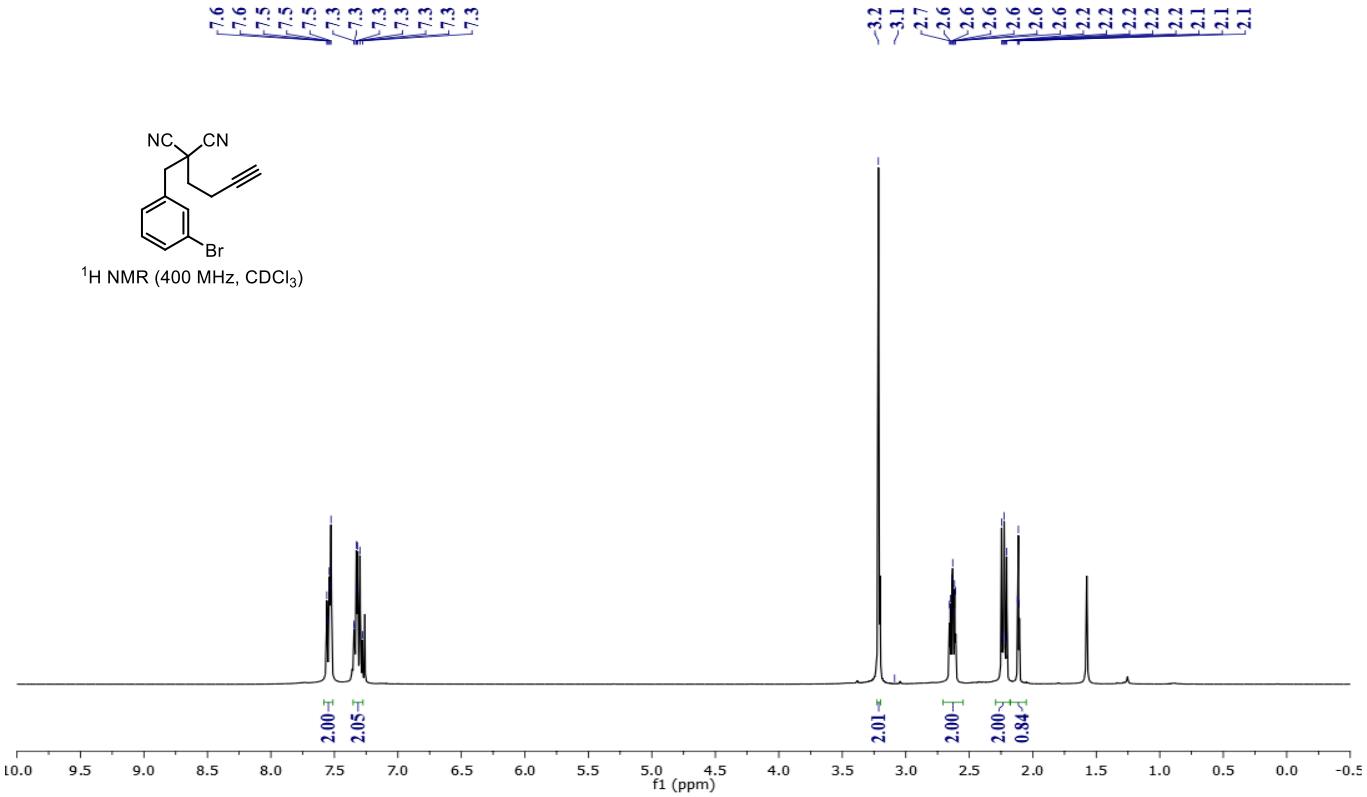
^{13}C NMR (75 MHz, $CDCl_3$)

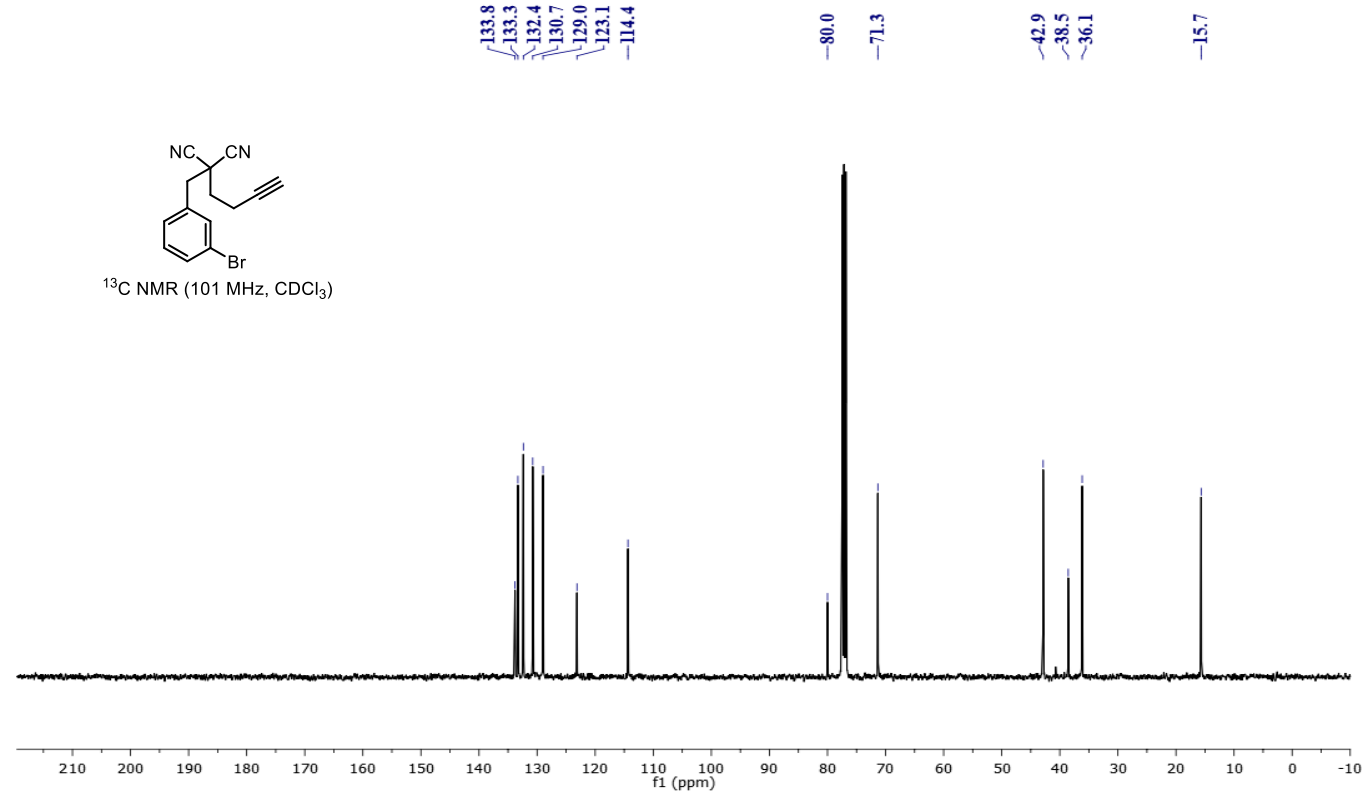
2-(But-3-yn-1-yl)-2-(3-chlorobenzyl)malononitrile (S9k):



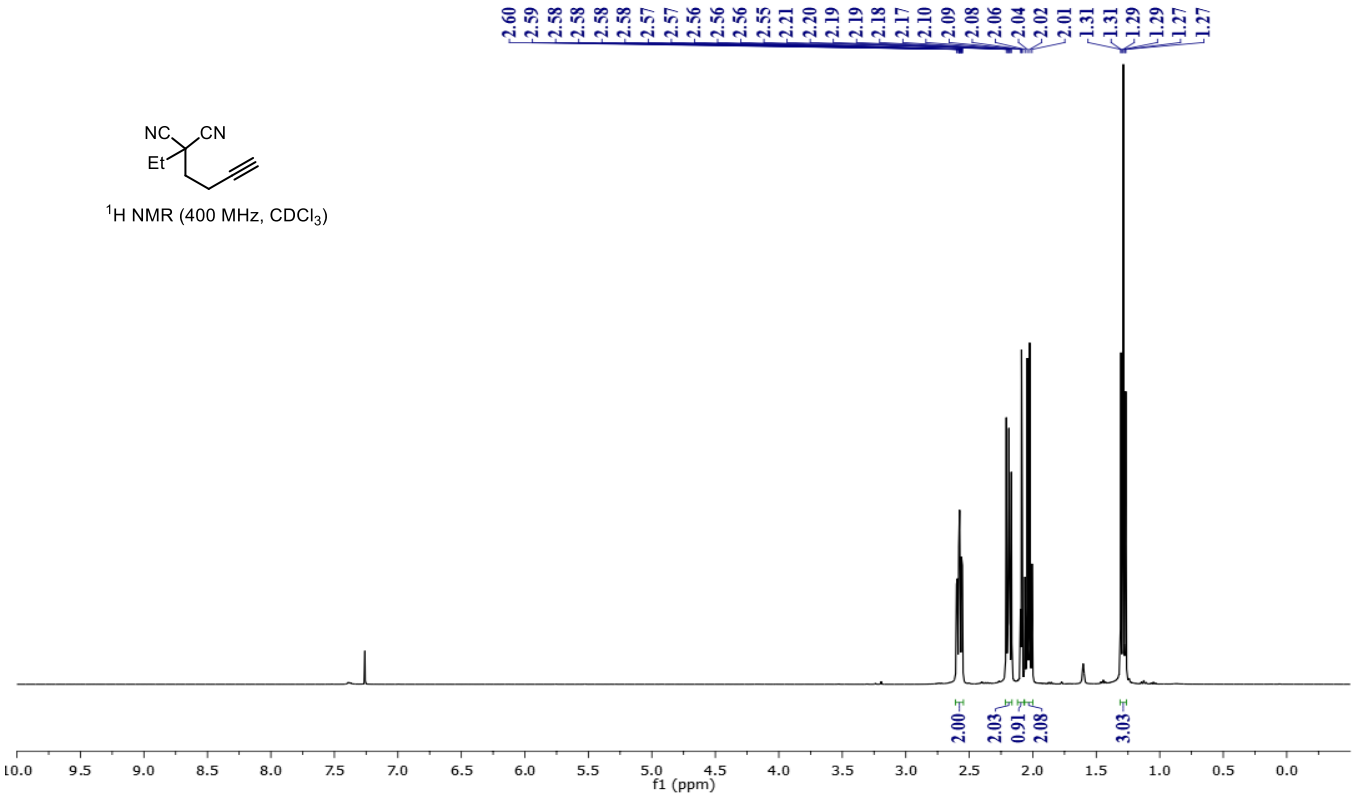


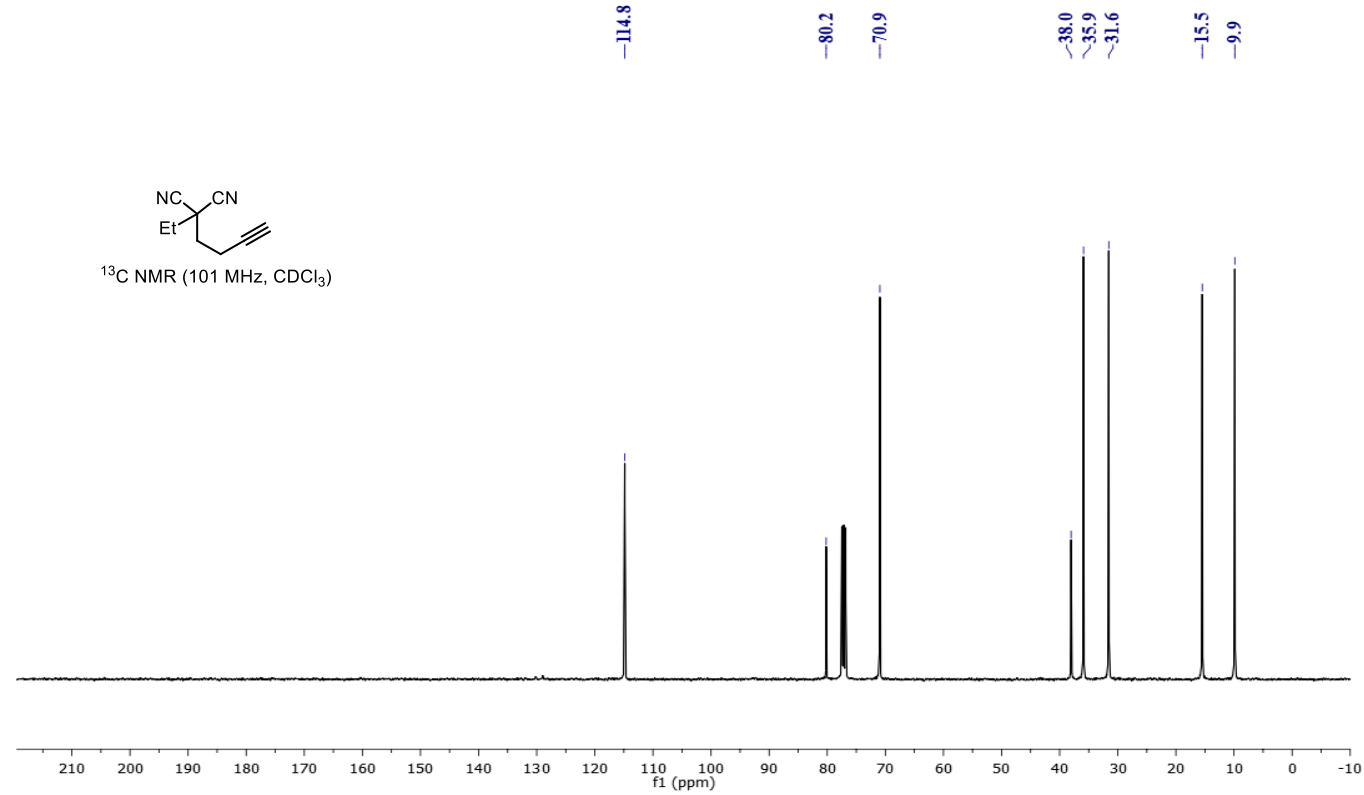
2-(3-Bromobenzyl)-2-(but-3-yn-1-yl)malononitrile (S9l):



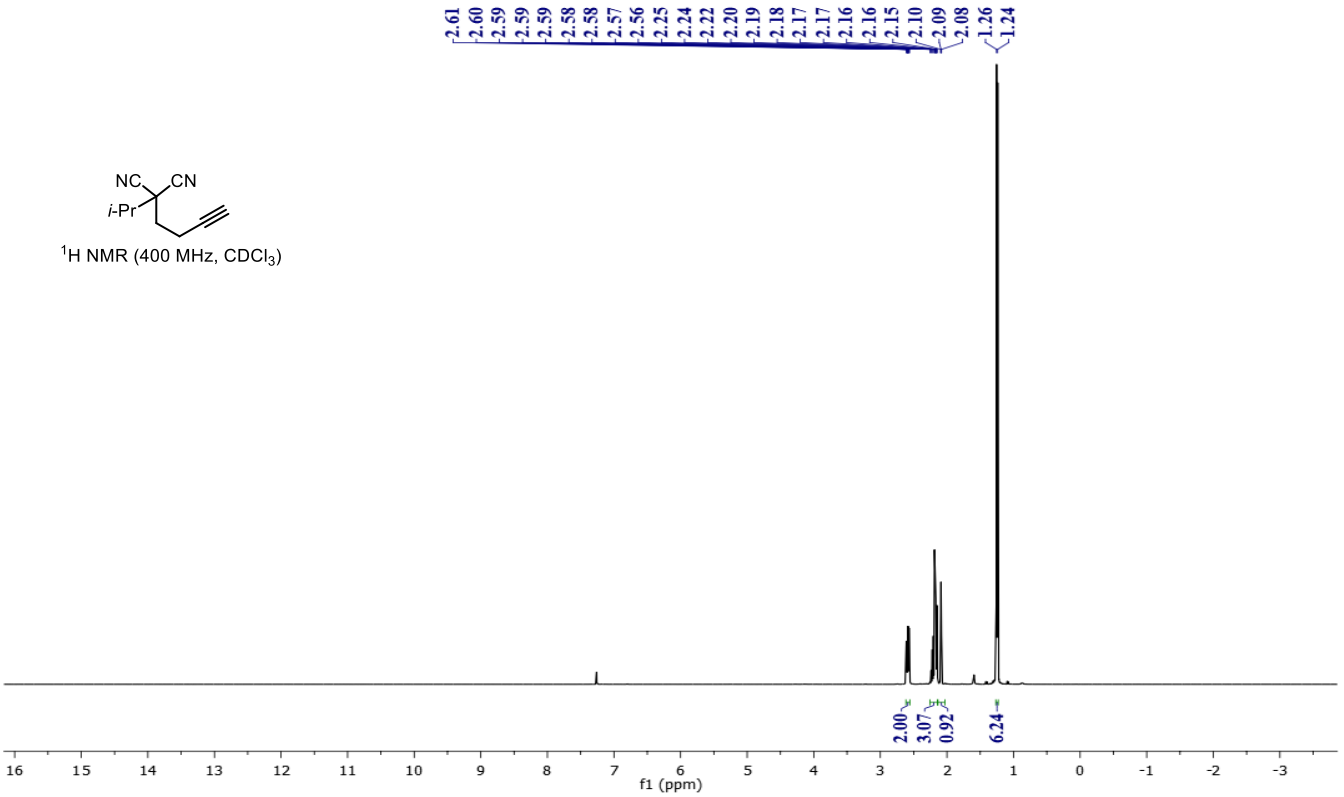


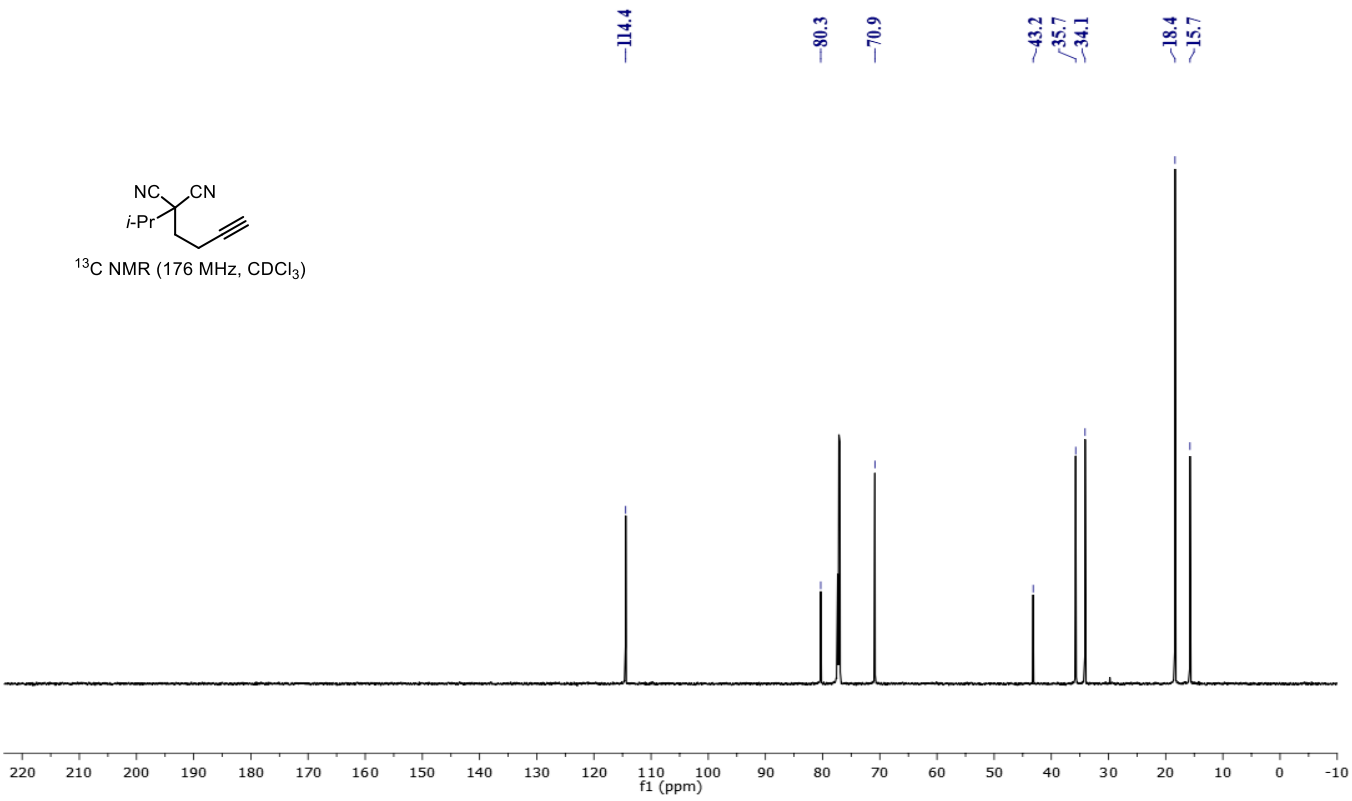
2-(But-3-yn-1-yl)-2-ethylmalononitrile (S9o):



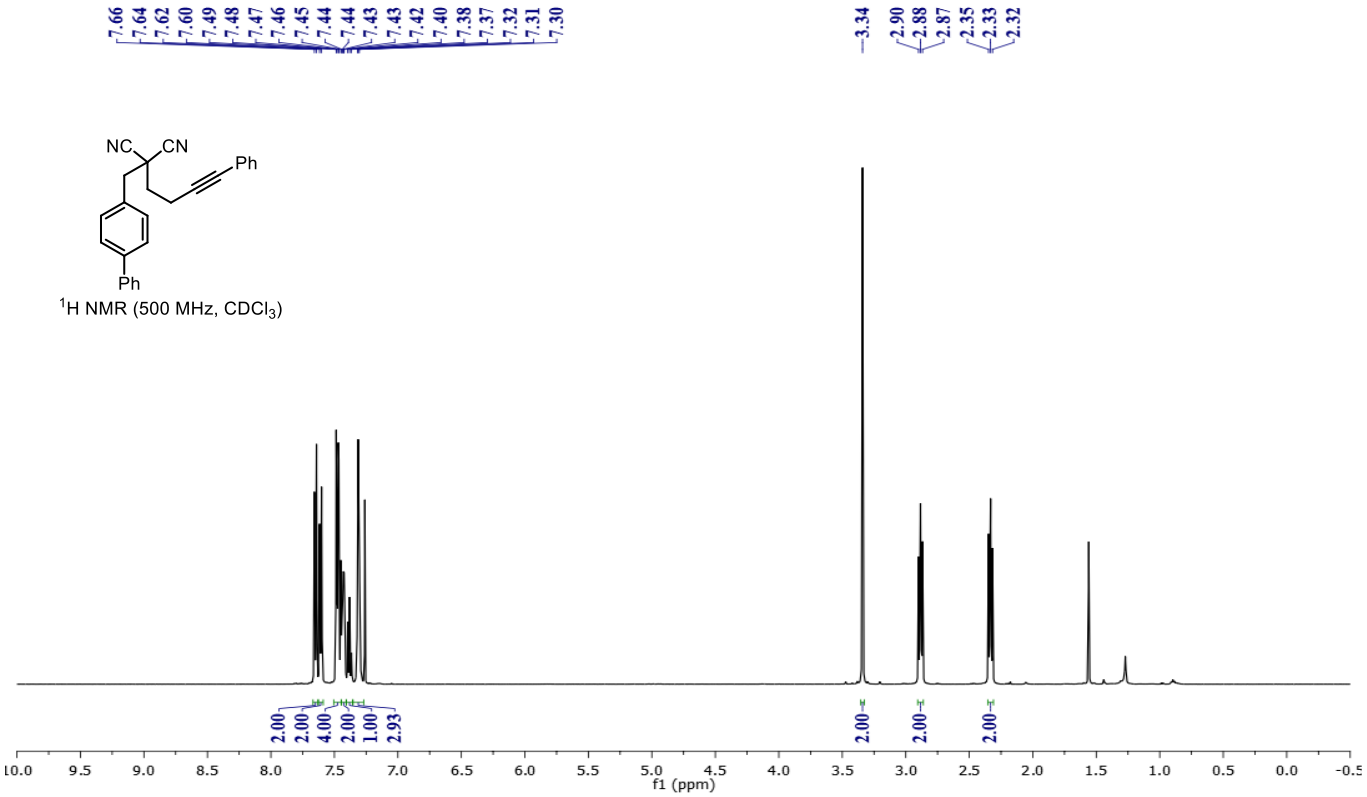


2-(But-3-yn-1-yl)-2-isopropylmalononitrile (S9p):

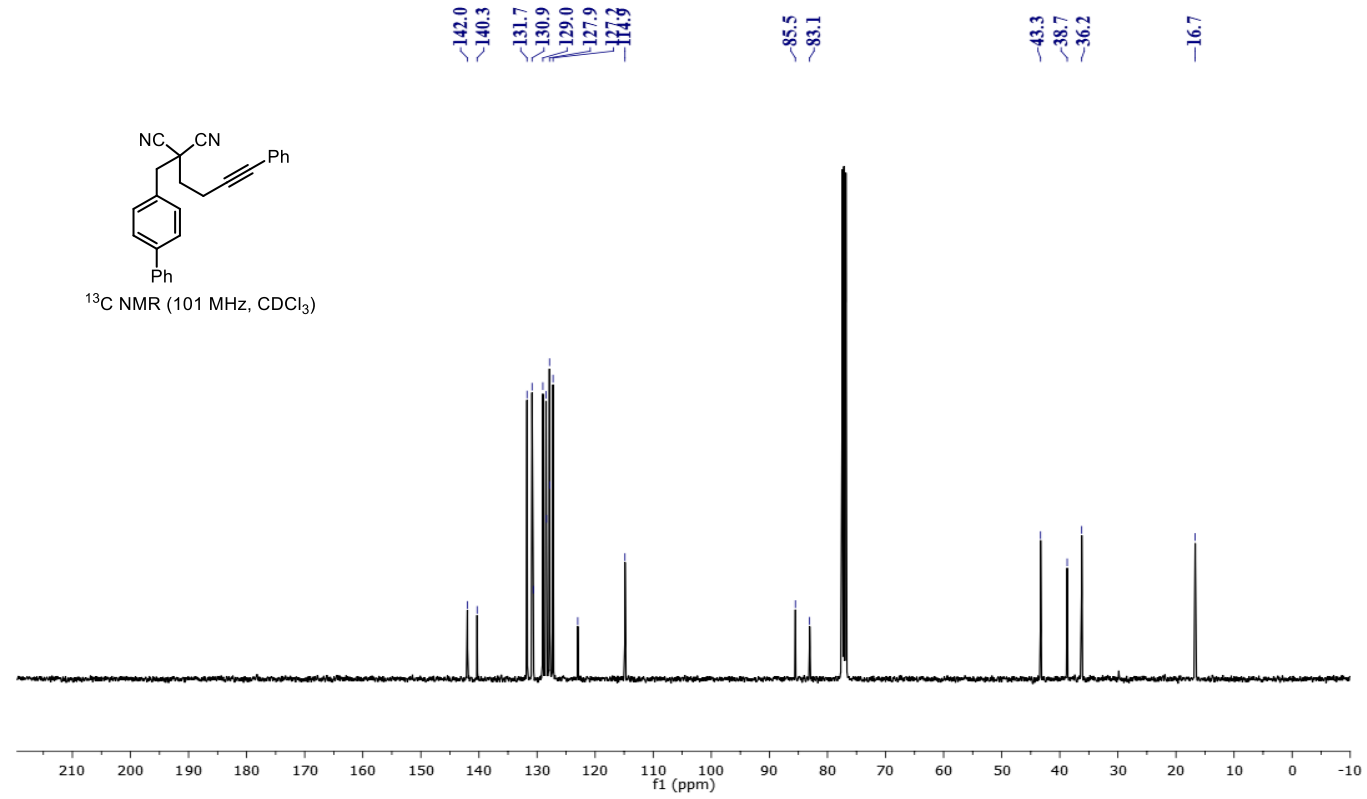




2-([1,1'-Biphenyl]-4-ylmethyl)-2-(4-phenylbut-3-yn-1-yl)malononitrile (1c):

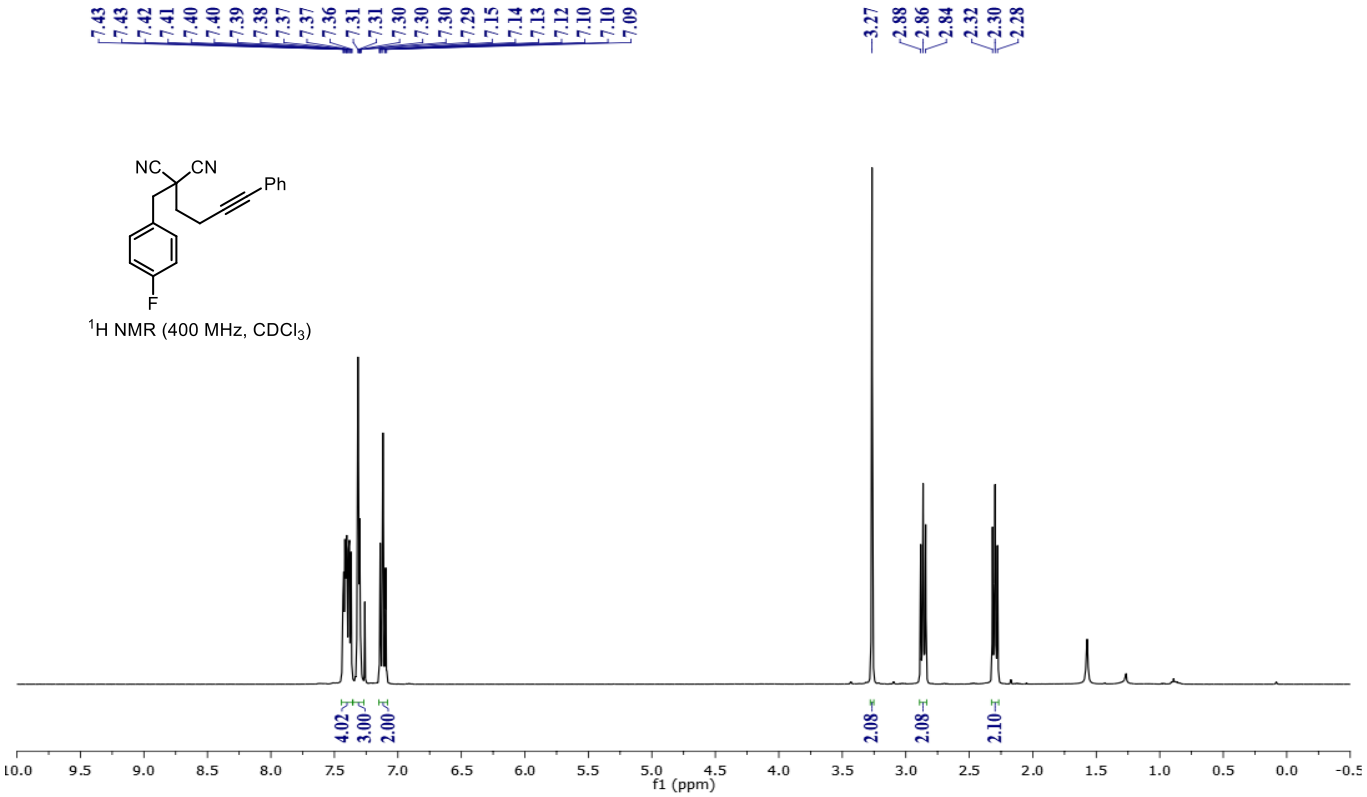


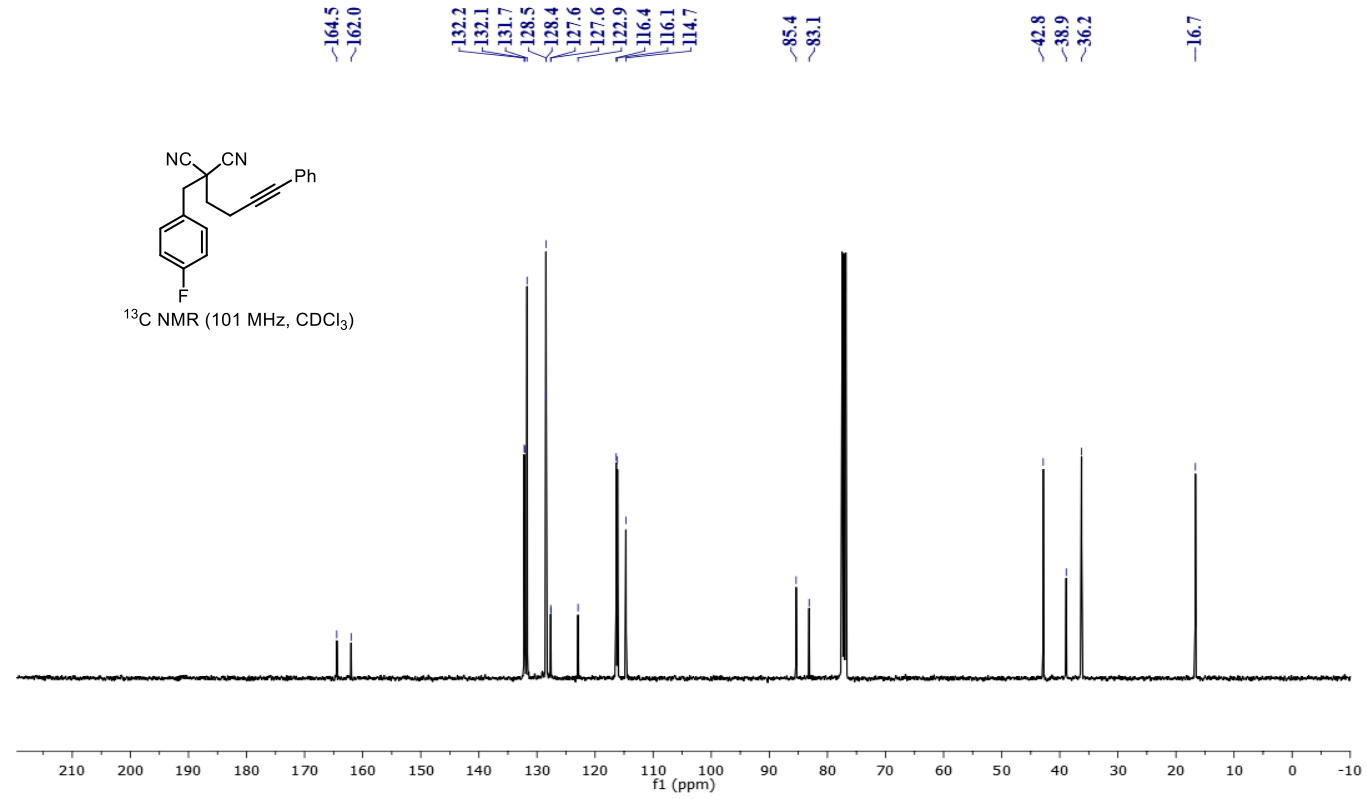
^{1}H NMR (500 MHz, $CDCl_3$)

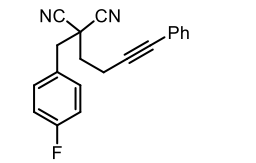


^{13}C NMR (101 MHz, $CDCl_3$)

2-(4-Fluorobenzyl)-2-(4-phenylbut-3-yn-1-yl)malononitrile (1d):

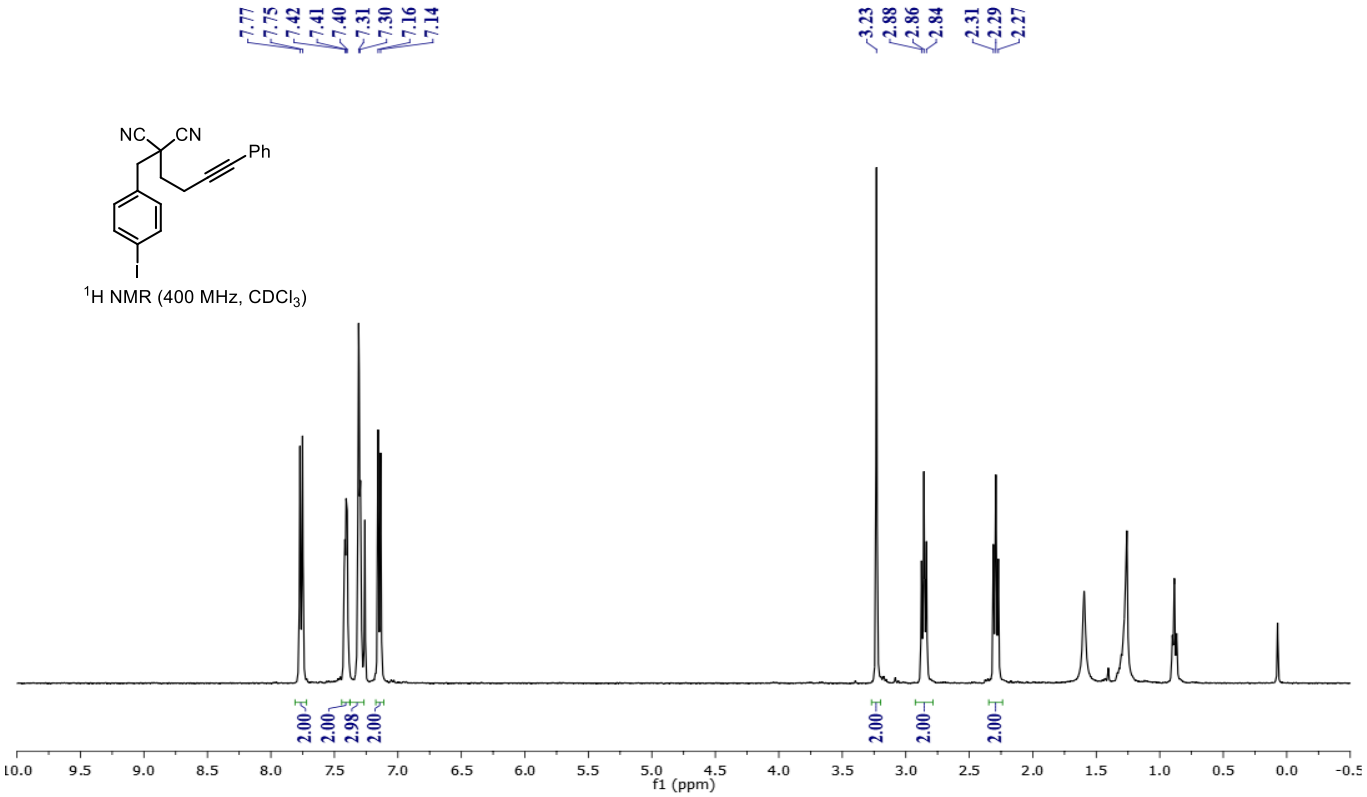


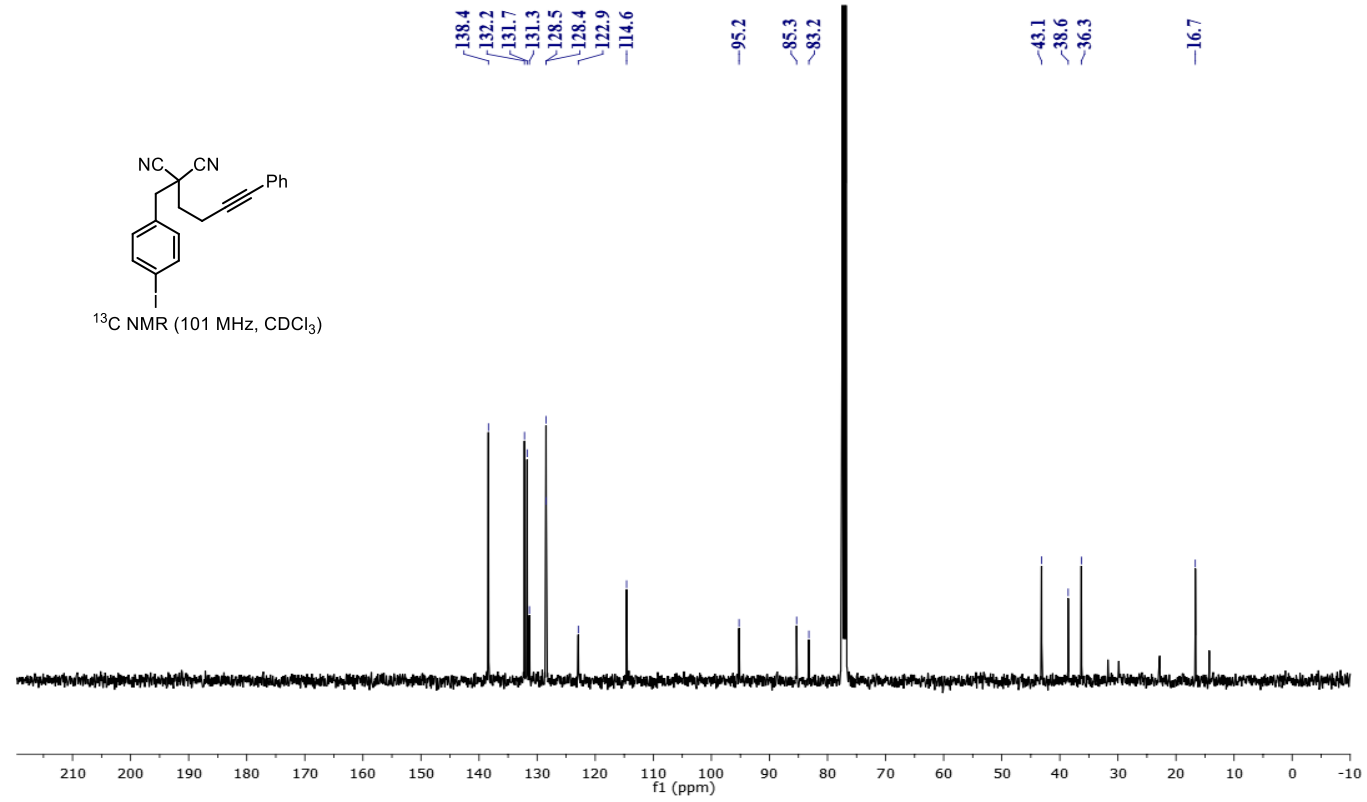




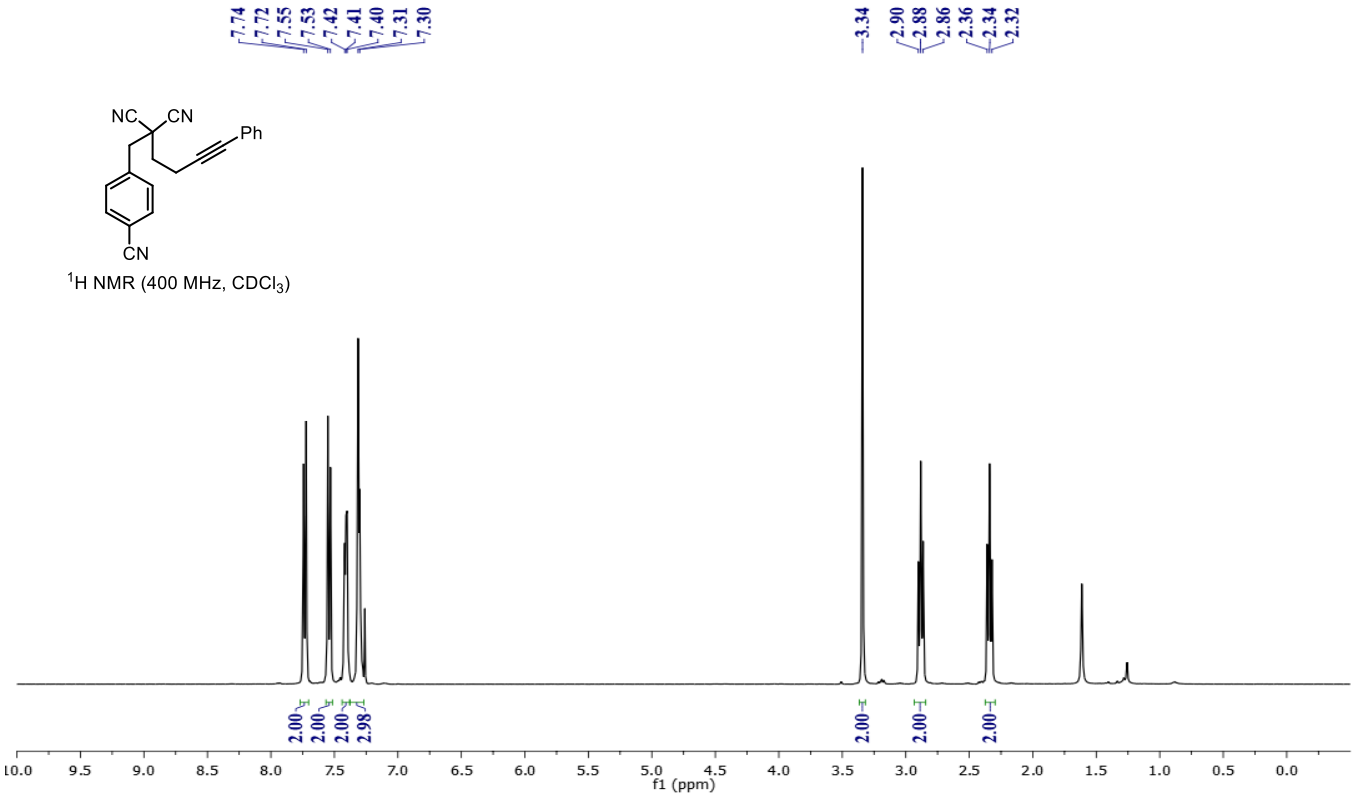
^{19}F NMR (377 MHz, $CDCl_3$)

2-(4-Iodobenzyl)-2-(4-phenylbut-3-yn-1-yl)malononitrile (1e):

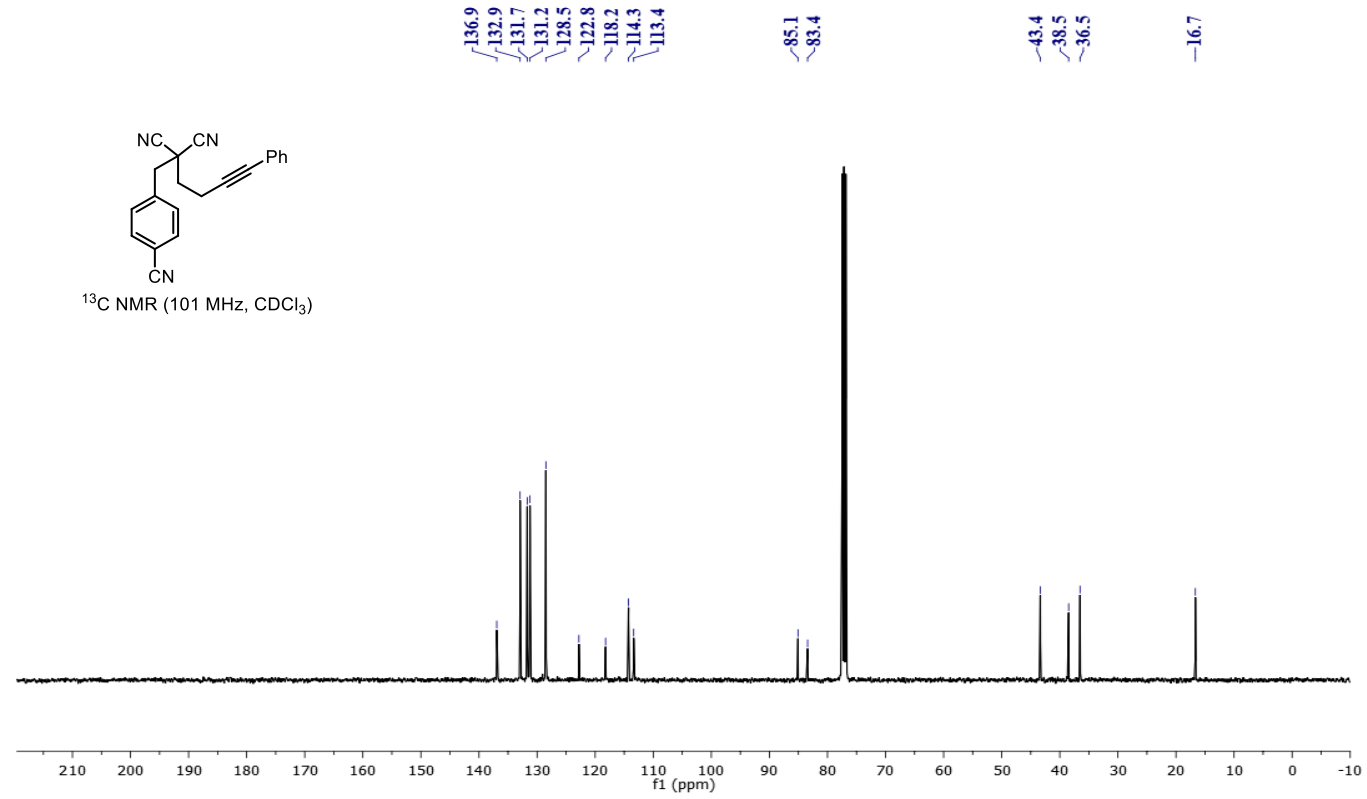




2-(4-Cyanobenzyl)-2-(4-phenylbut-3-yn-1-yl)malononitrile (1f):

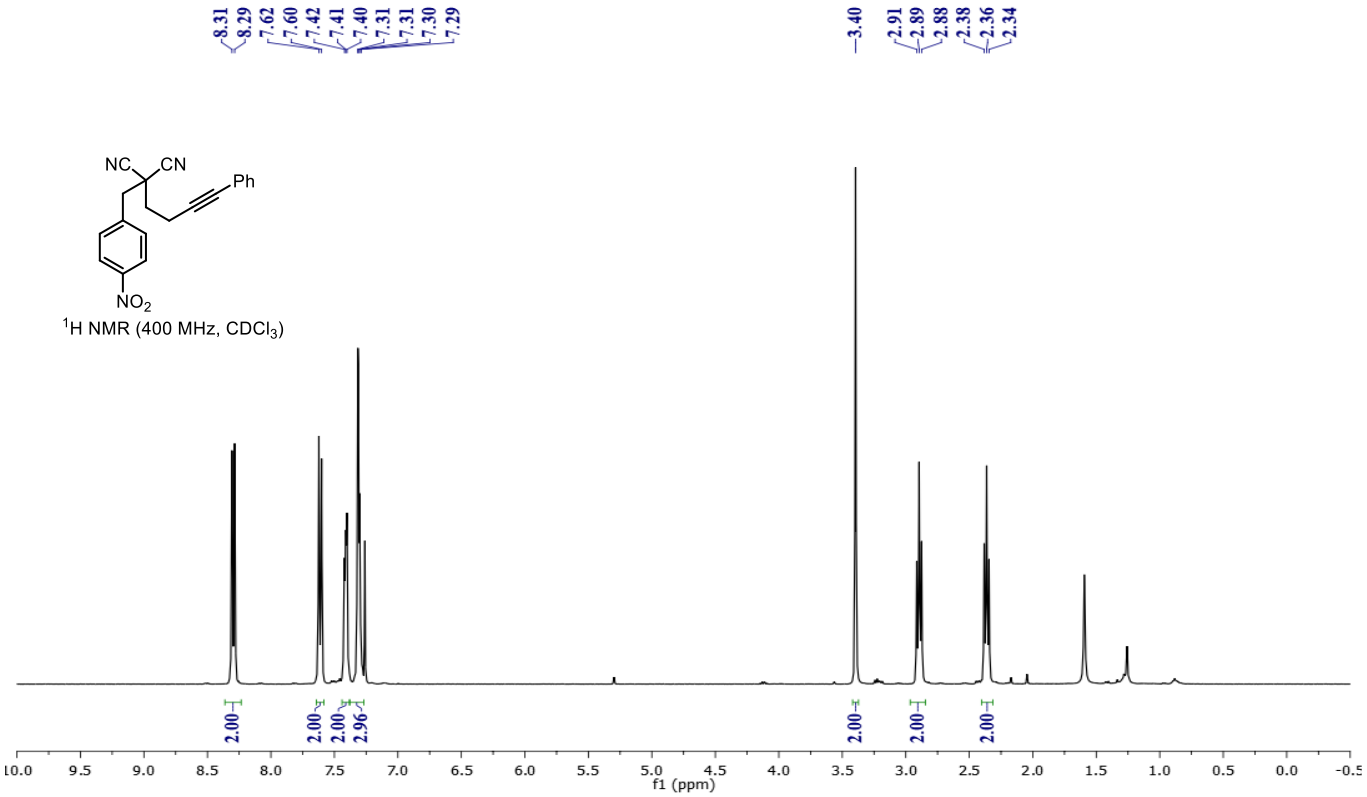


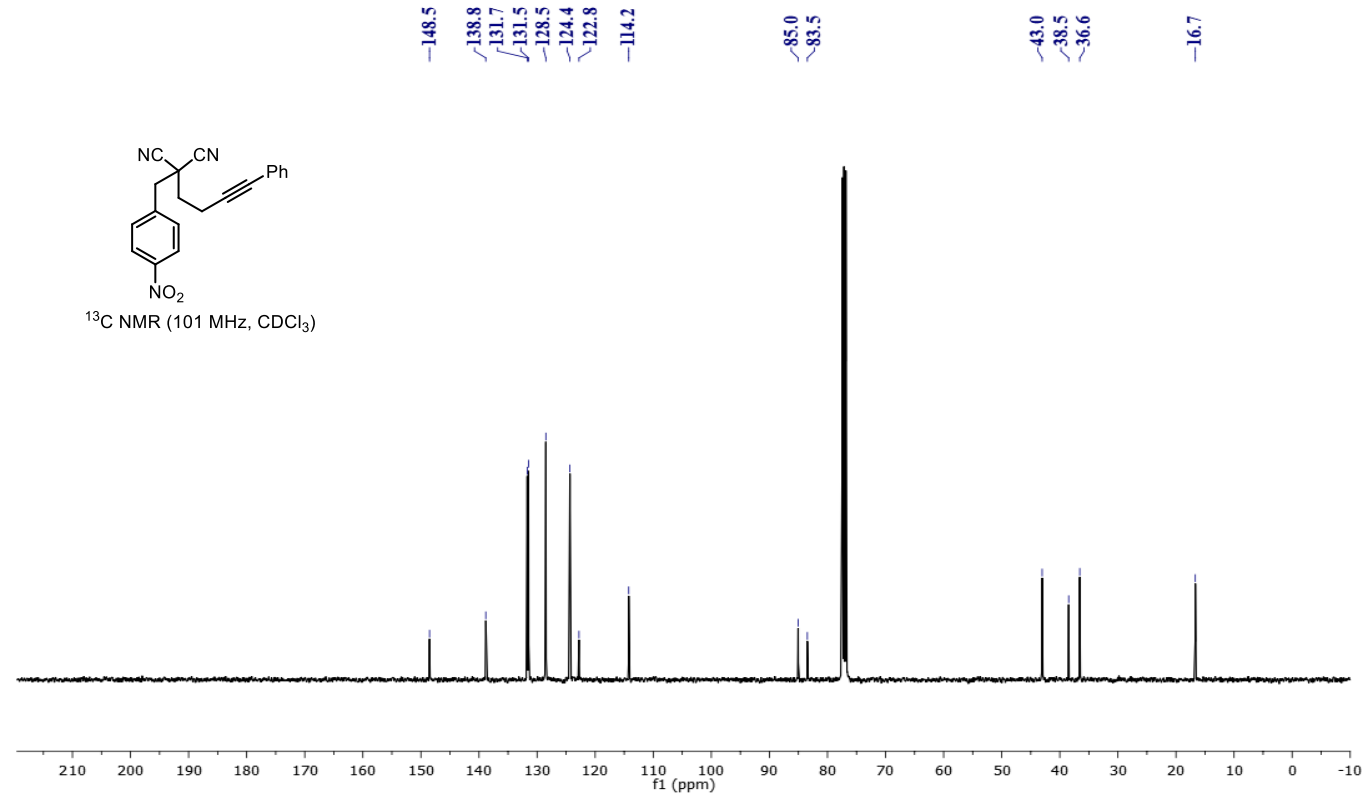
^{1}H NMR (400 MHz, $CDCl_3$)



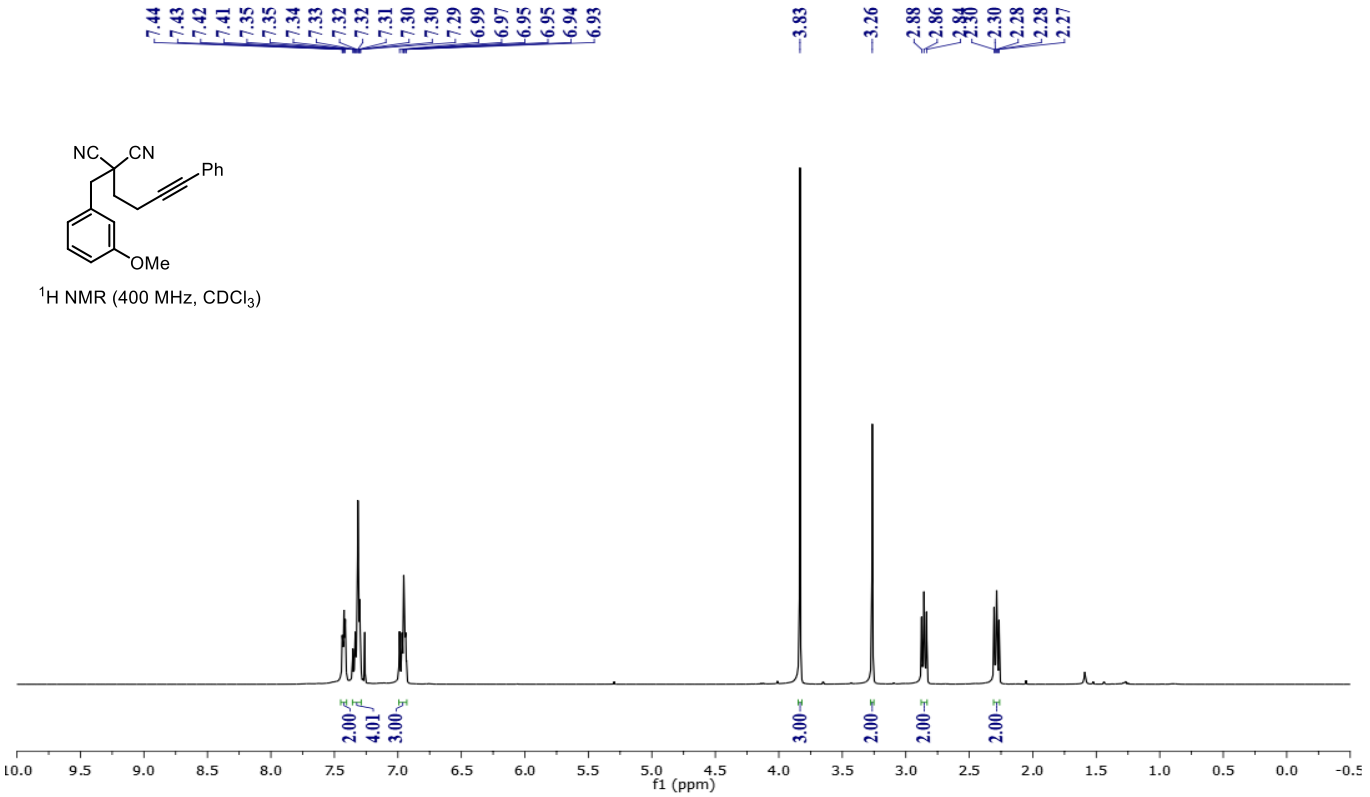
^{13}C NMR (101 MHz, $CDCl_3$)

2-(4-Nitrobenzyl)-2-(4-phenylbut-3-yn-1-yl)malononitrile (1g):

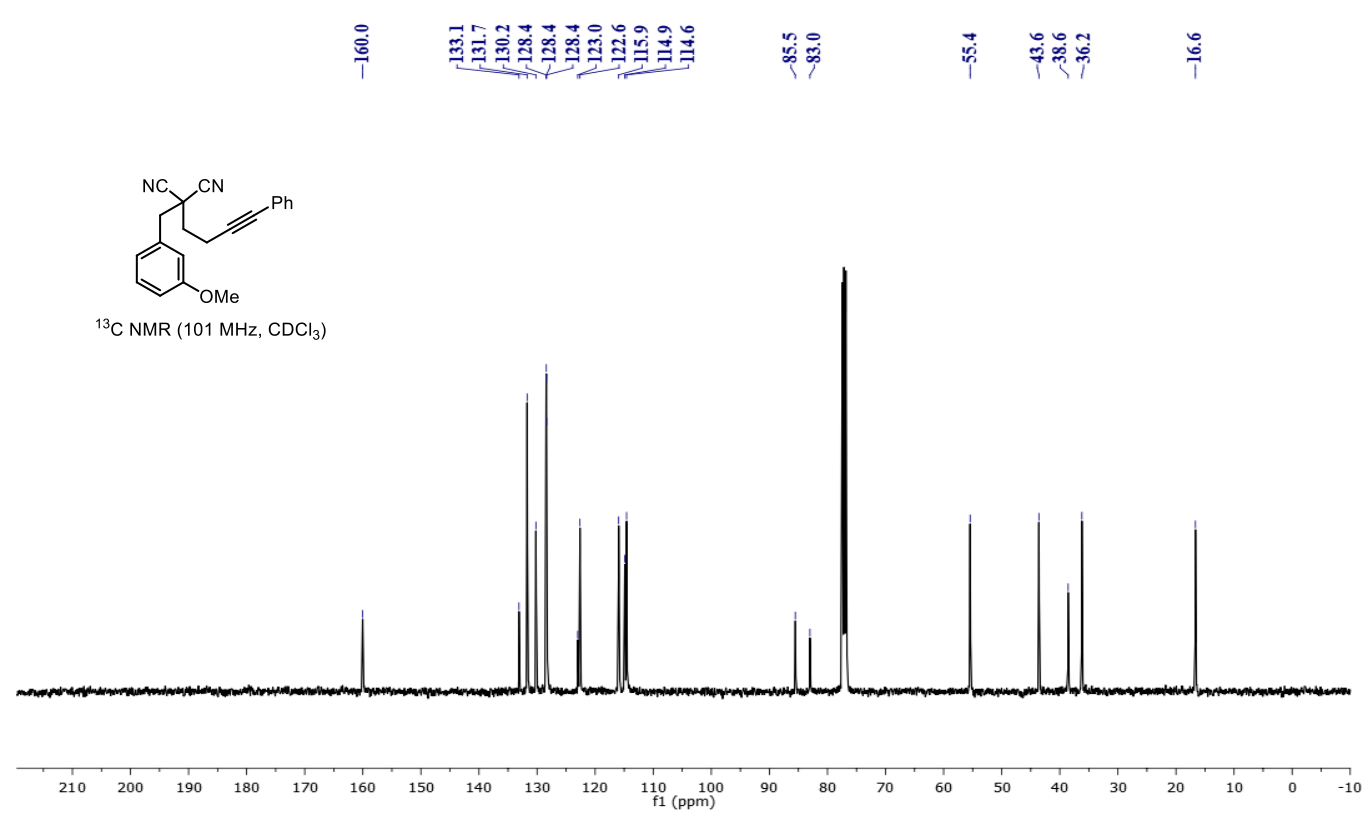




2-(3-Methoxybenzyl)-2-(4-phenylbut-3-yn-1-yl)malononitrile (1j):

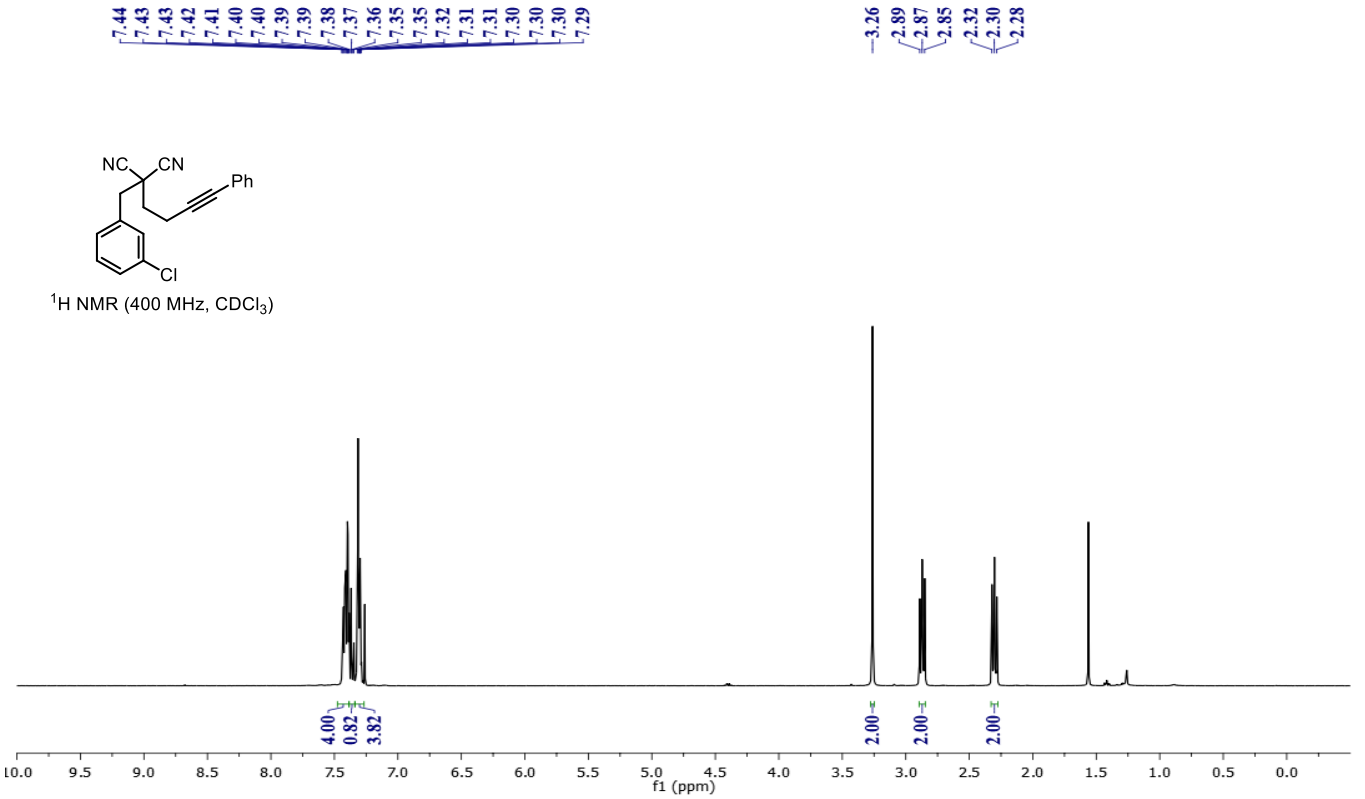


^{1}H NMR (400 MHz, $CDCl_3$)

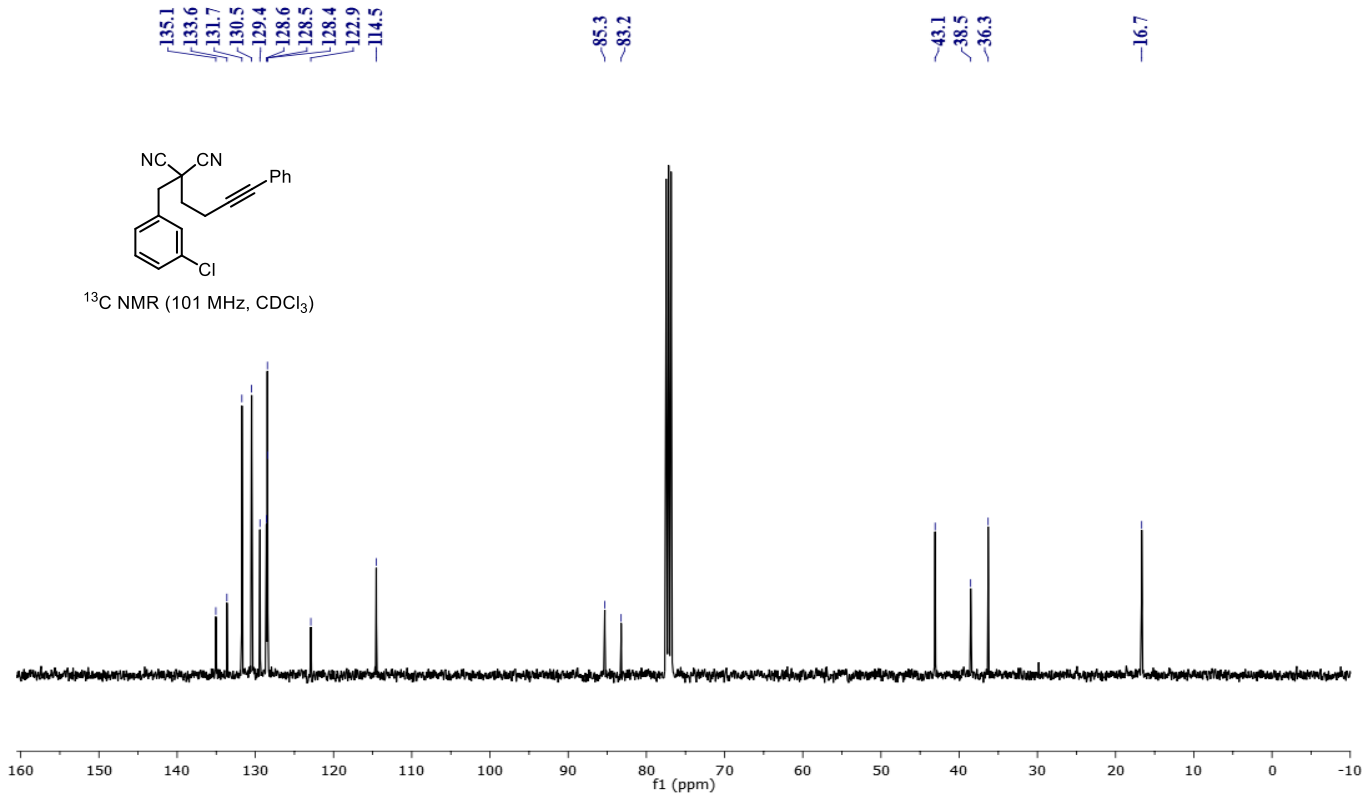


^{13}C NMR (101 MHz, $CDCl_3$)

2-(3-Chlorobenzyl)-2-(4-phenylbut-3-yn-1-yl)malononitrile (1k):

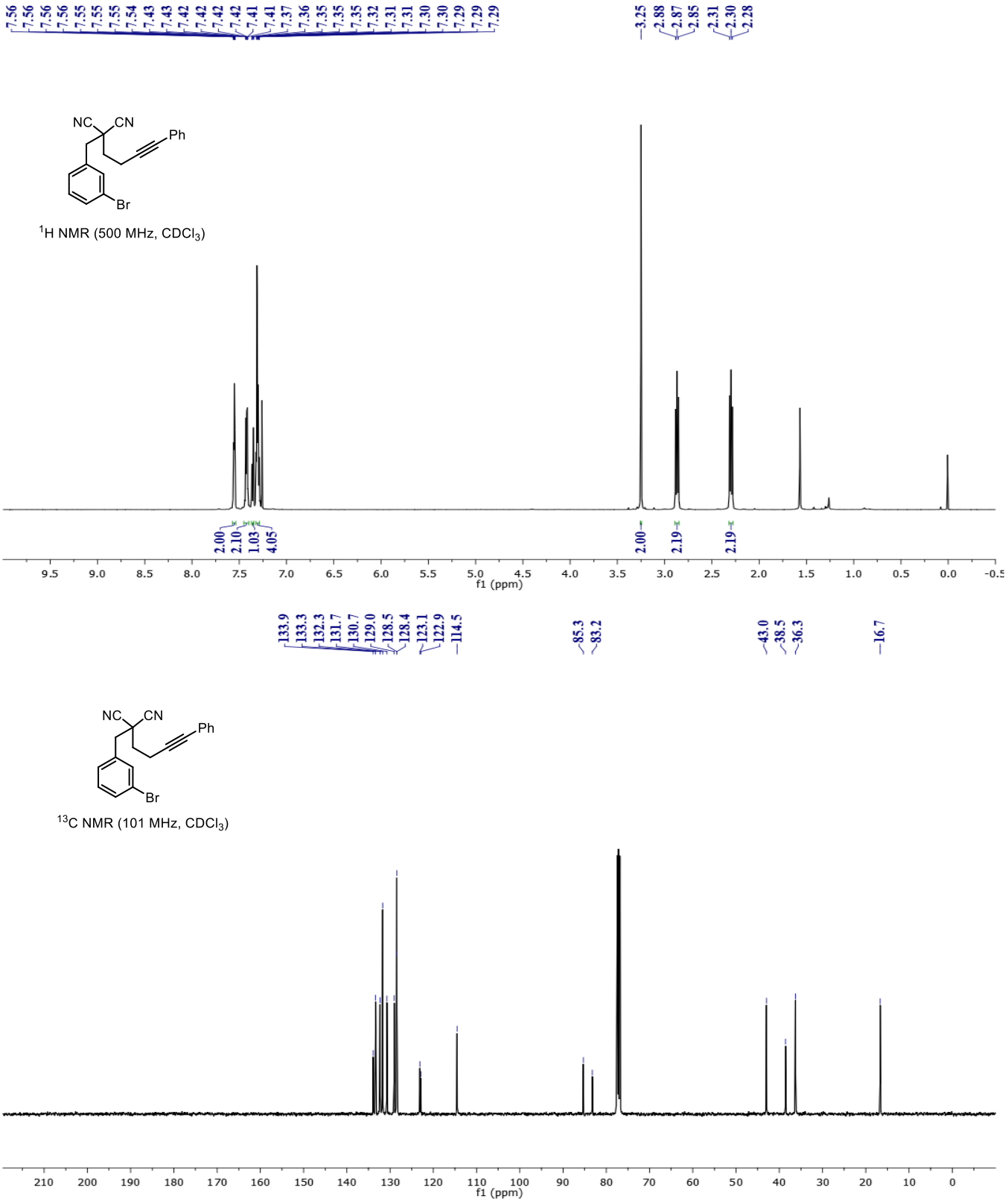


^{1}H NMR (400 MHz, $CDCl_3$)

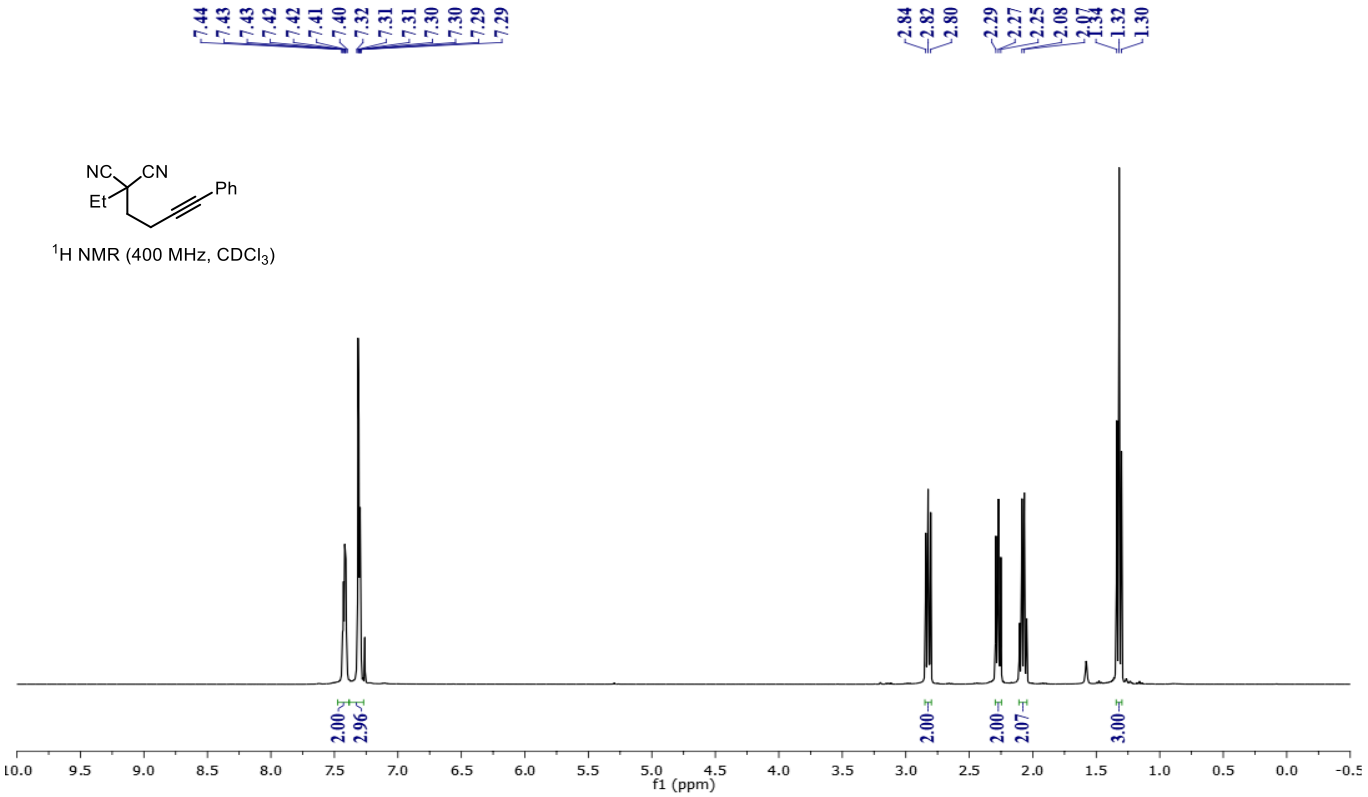


^{13}C NMR (101 MHz, $CDCl_3$)

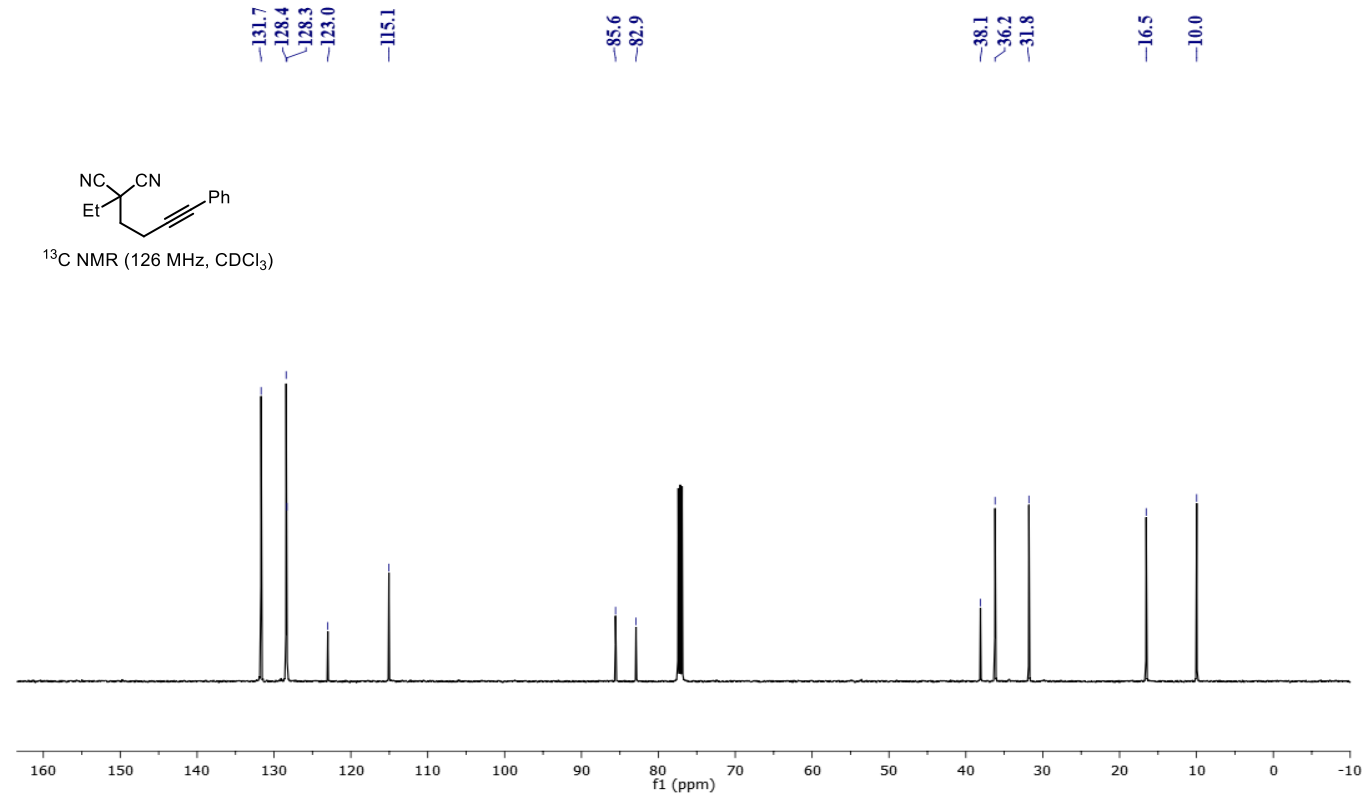
2-(3-Bromobenzyl)-2-(4-phenylbut-3-yn-1-yl)malononitrile (1l):



2-Ethyl-2-(4-phenylbut-3-yn-1-yl)malononitrile (1o):

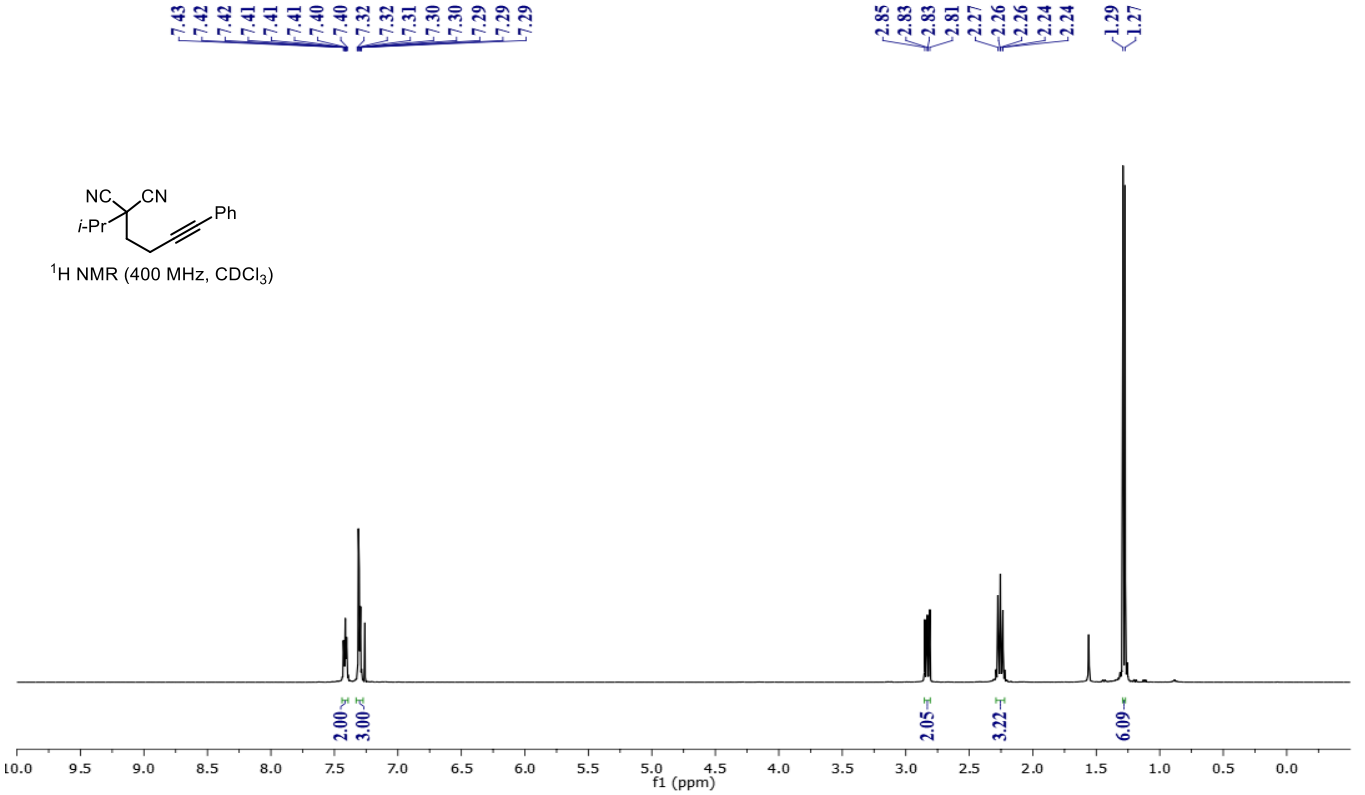


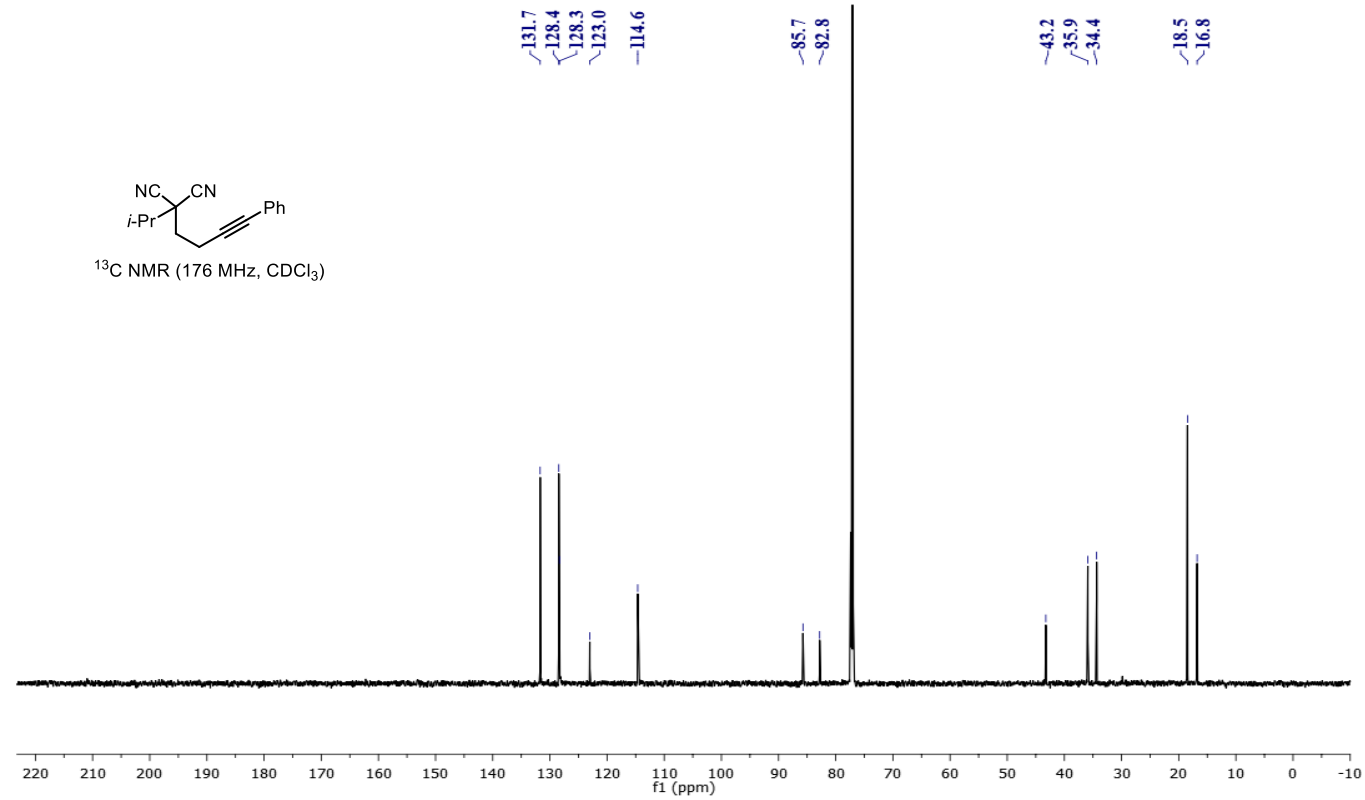
^{1}H NMR (400 MHz, $CDCl_3$)



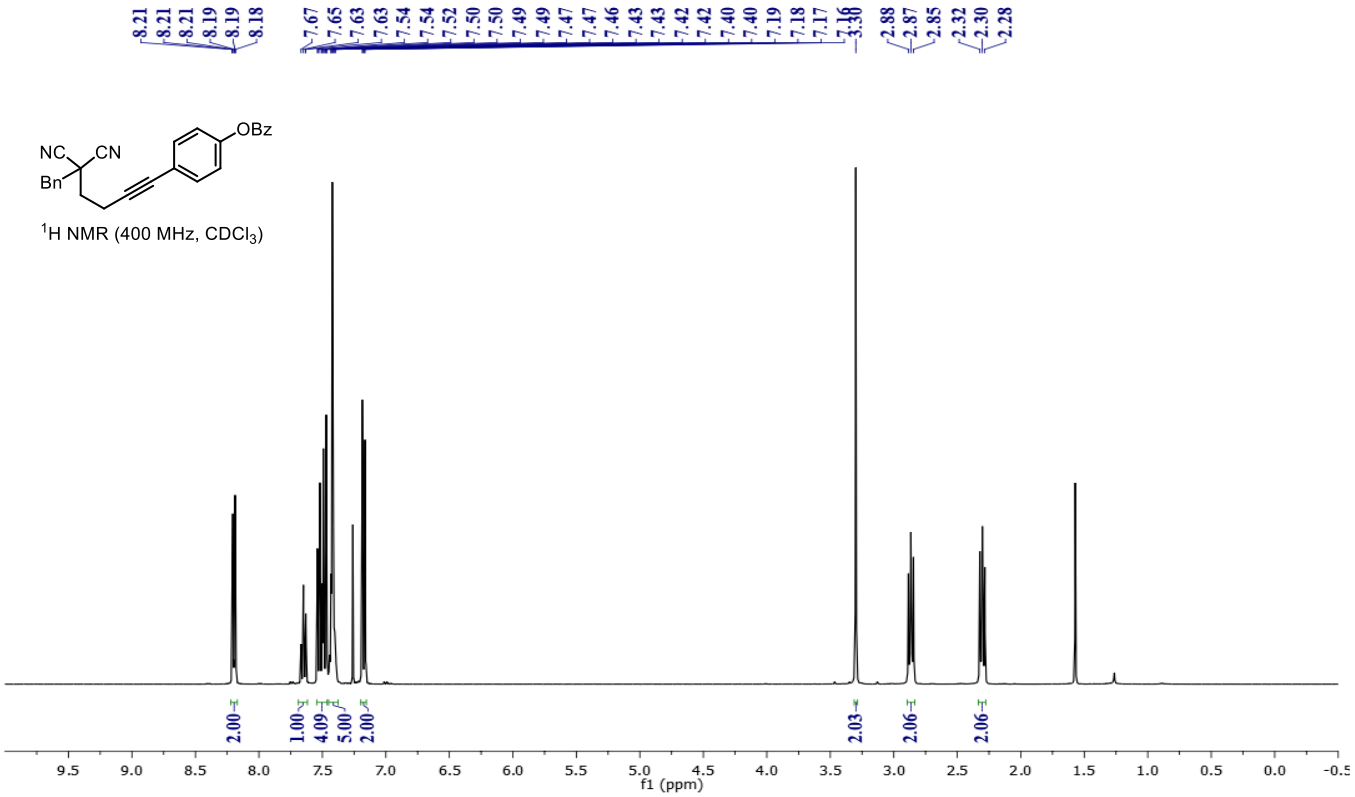
^{13}C NMR (126 MHz, $CDCl_3$)

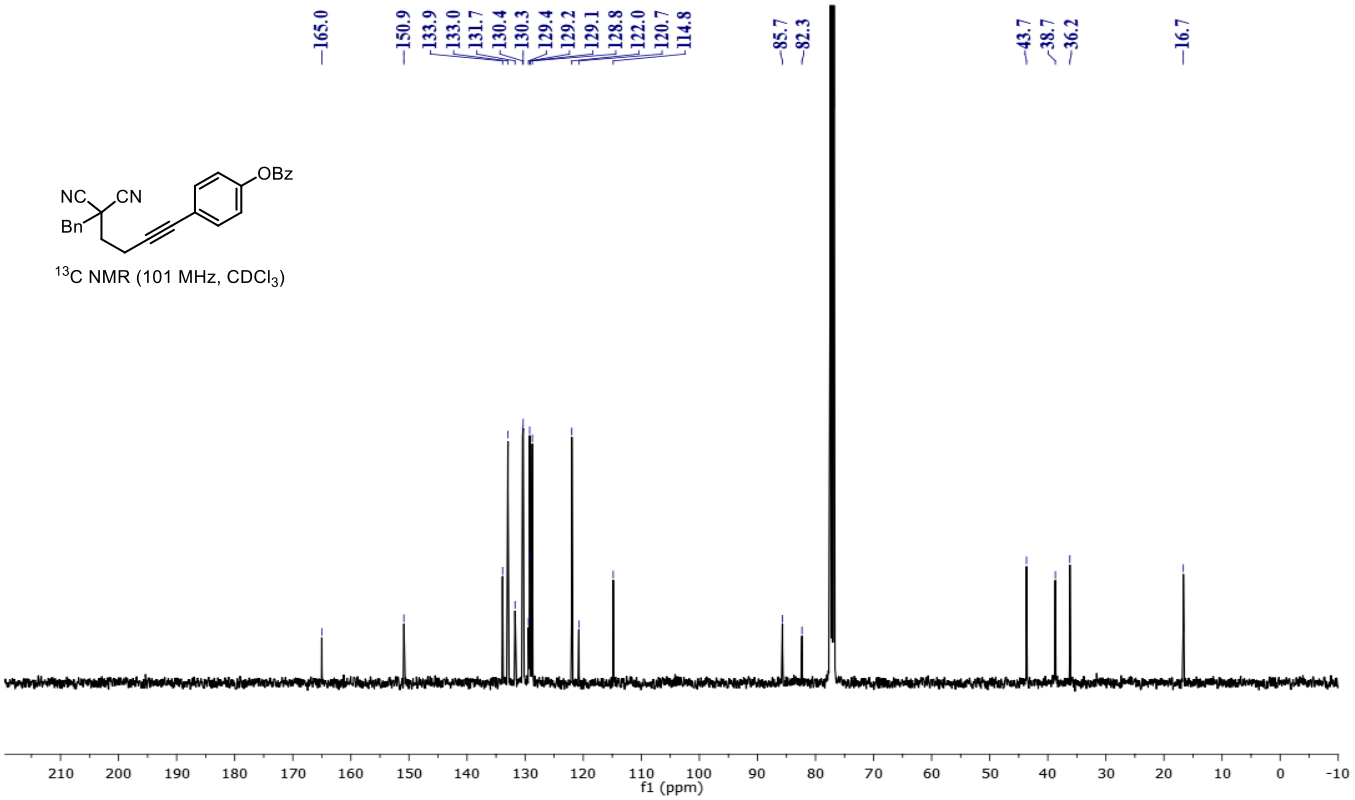
2-Isopropyl-2-(4-phenylbut-3-yn-1-yl)malononitrile (1p):



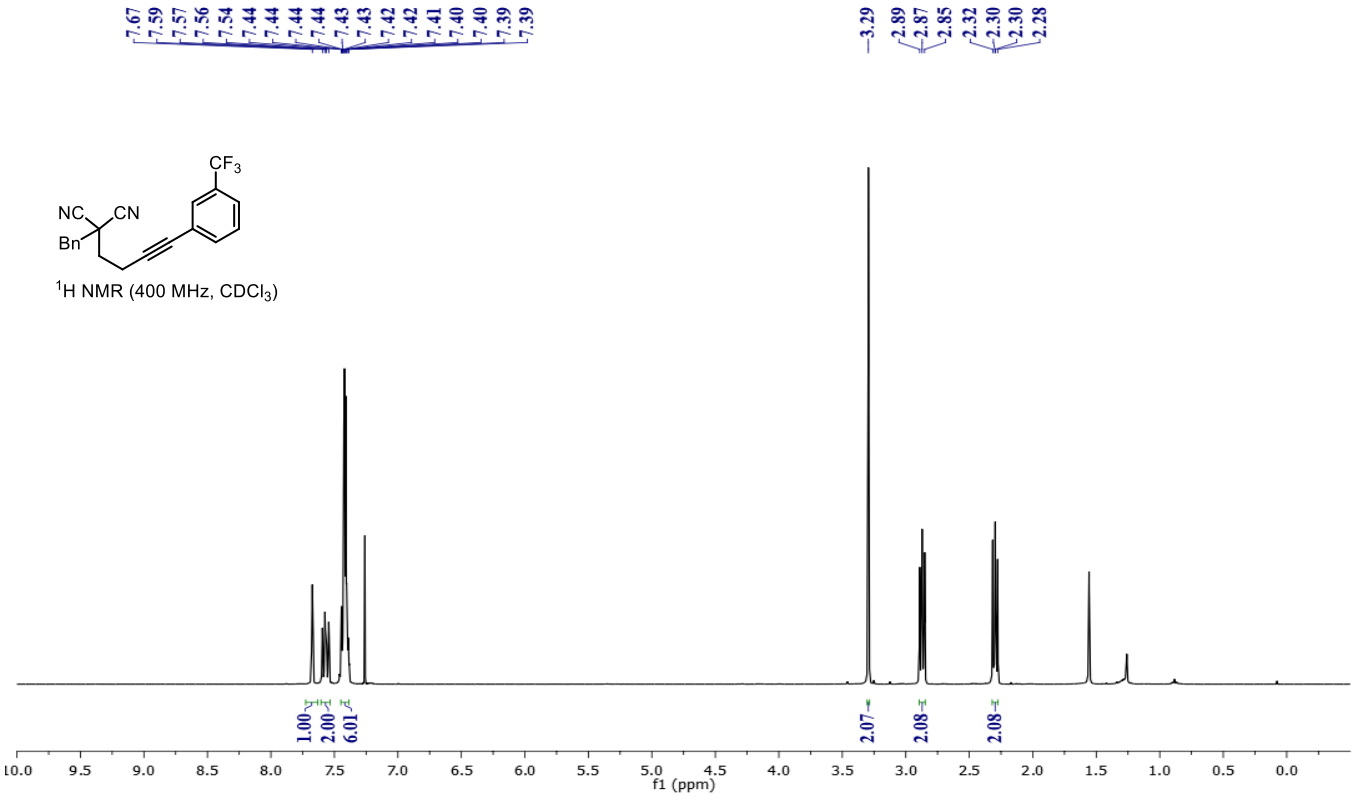


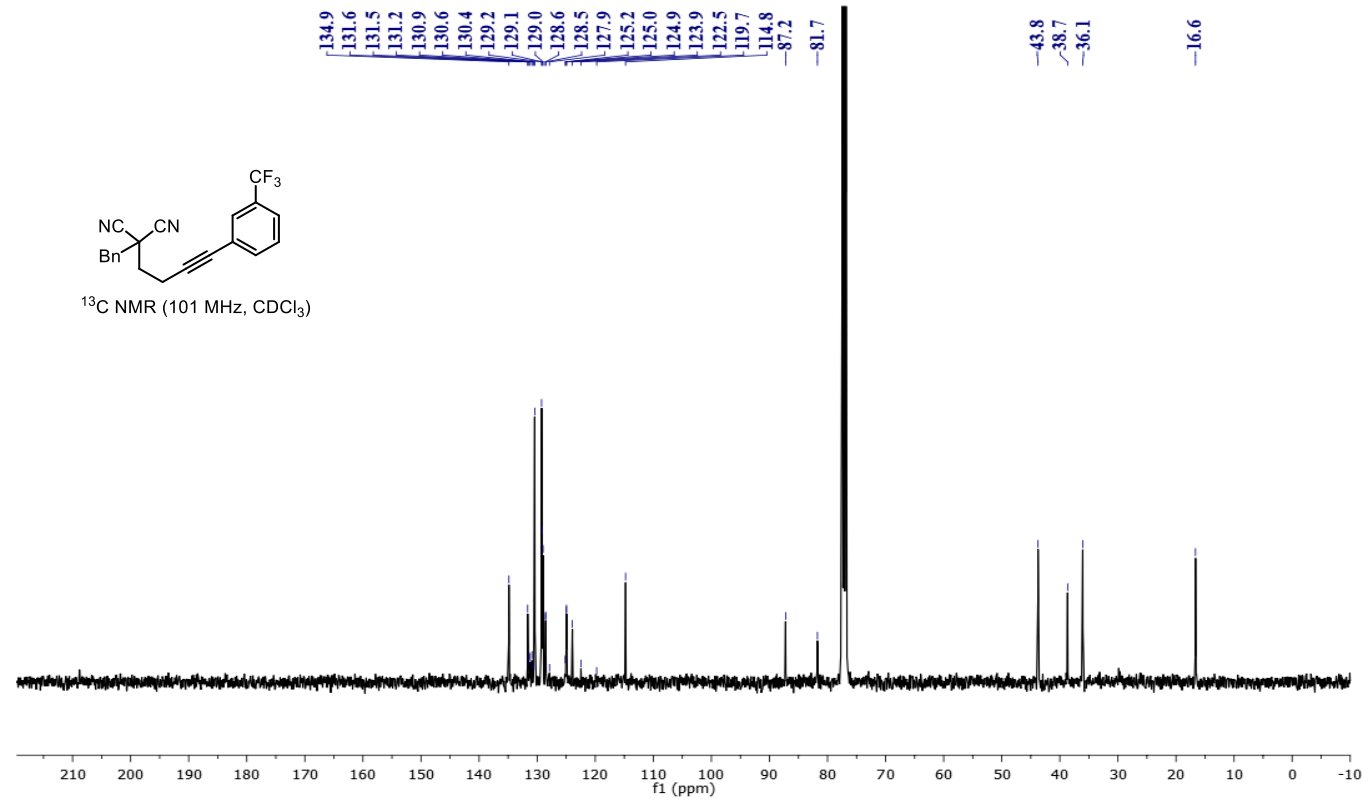
4-(5,5-Dicyano-6-phenylhex-1-yn-1-yl)phenyl benzoate (1y):

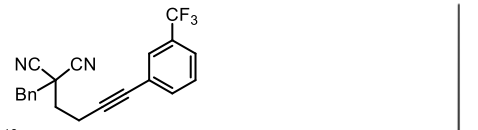




2-Benzyl-2-(4-(3-(trifluoromethyl)phenyl)but-3-yn-1-yl)malononitrile (1z):

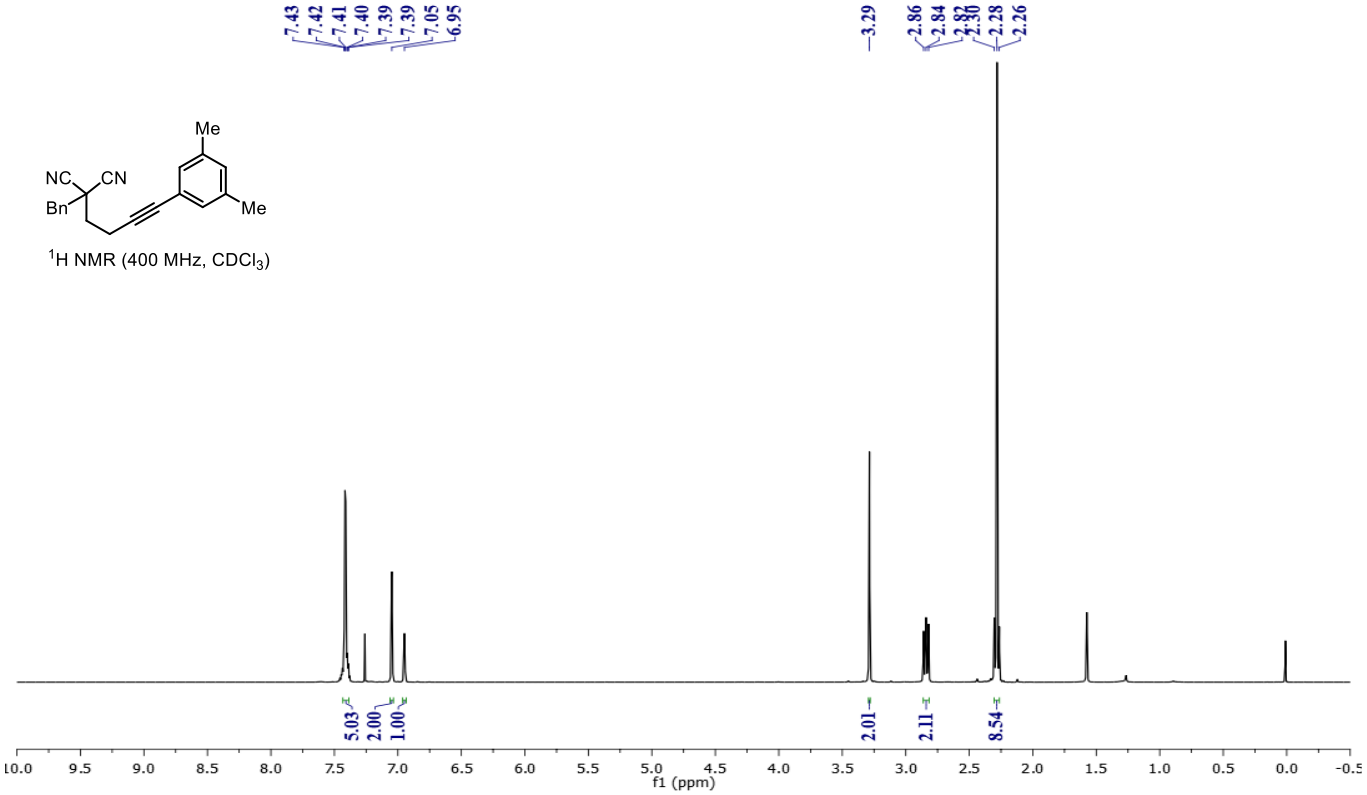


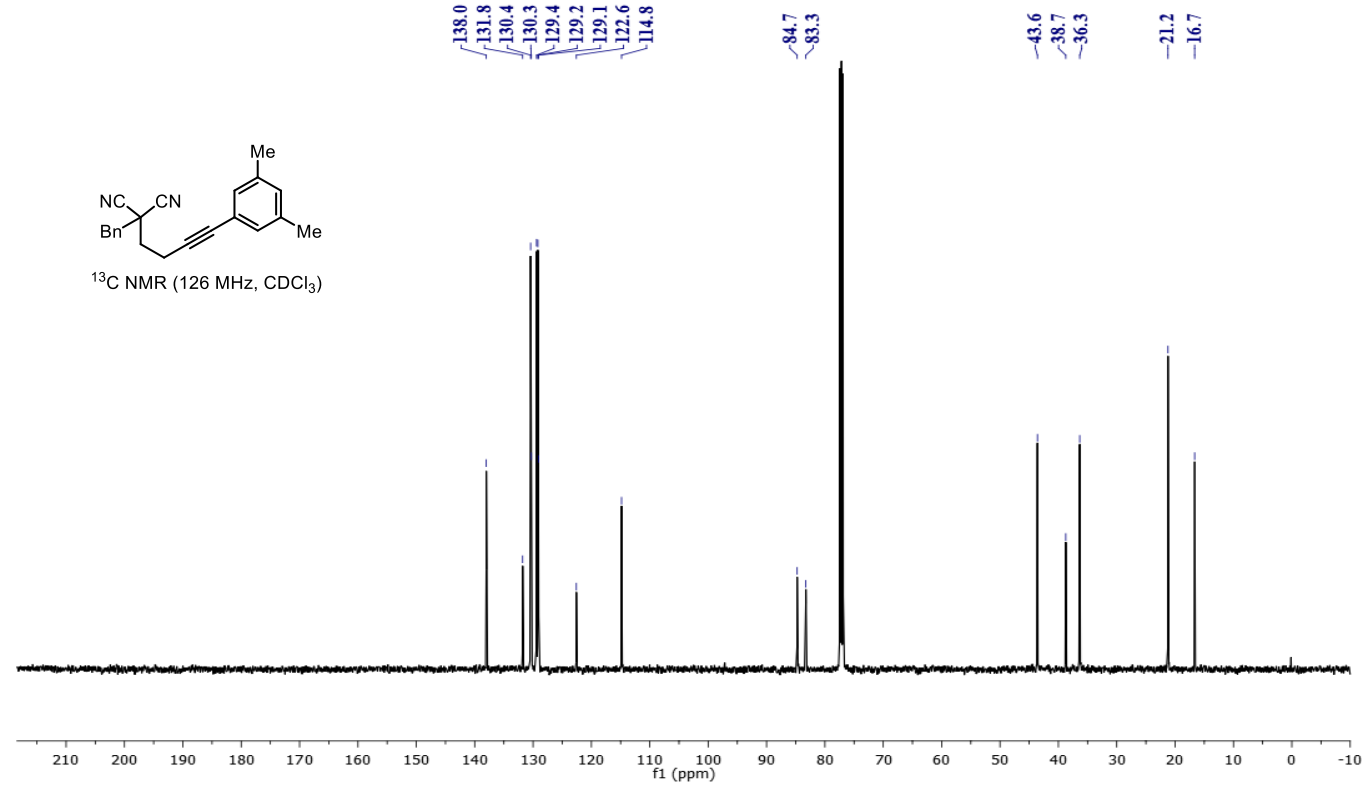




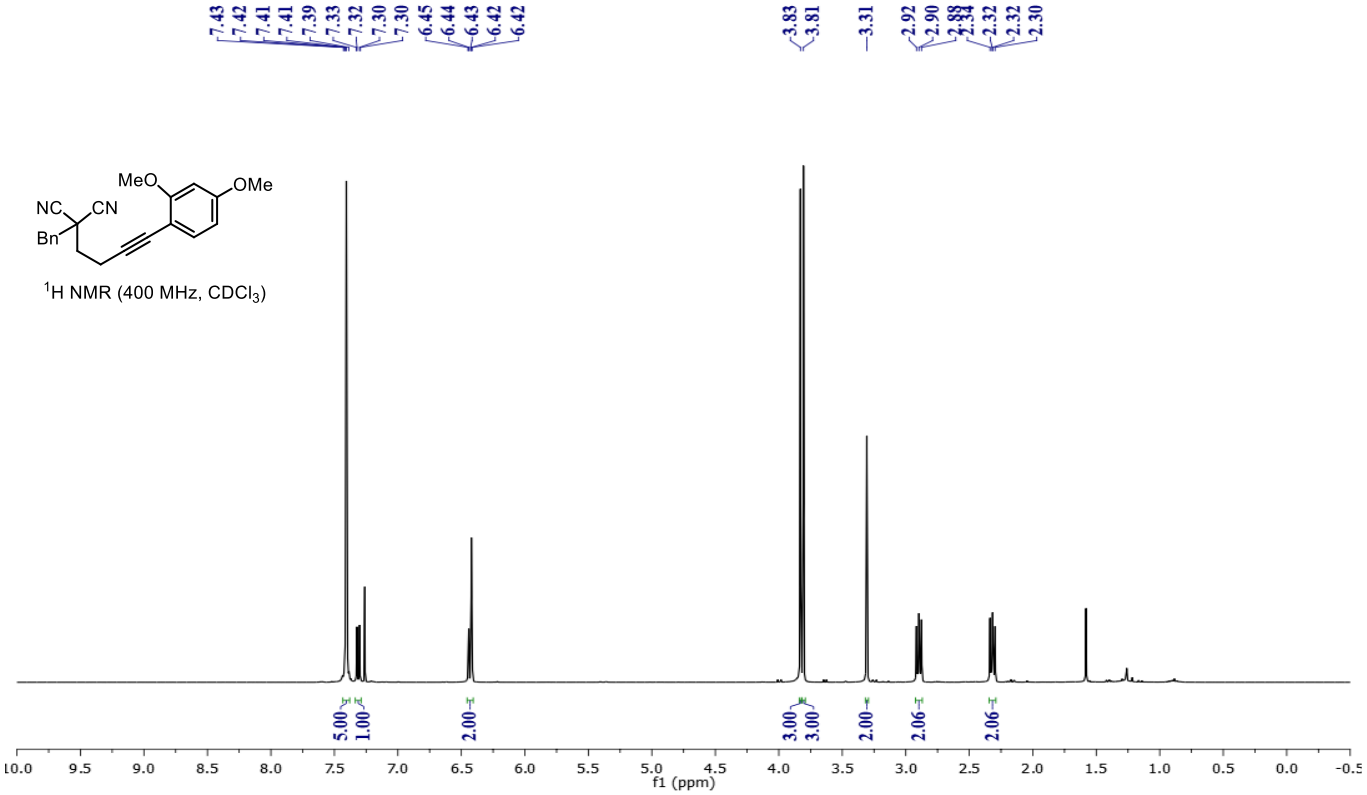
^{19}F NMR (377 MHz, $CDCl_3$)

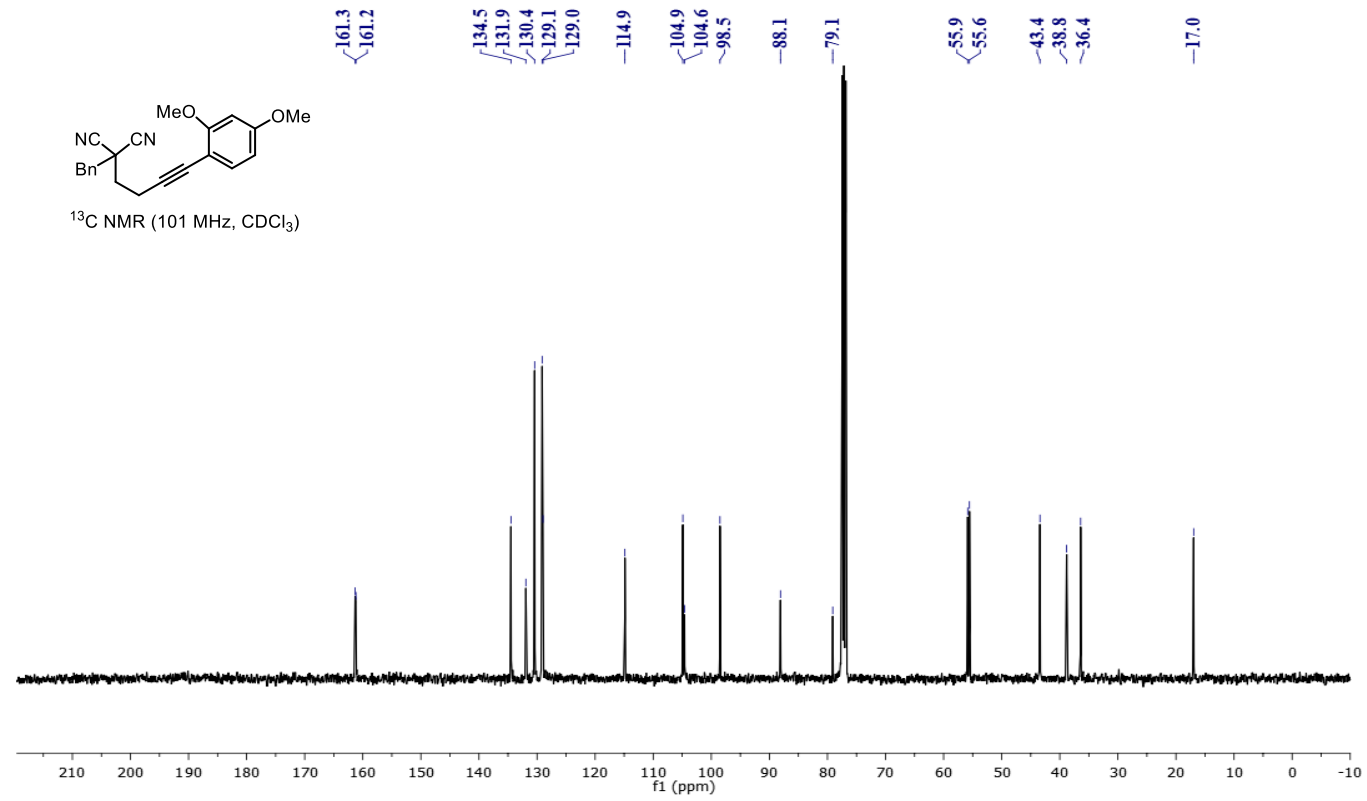
2-Benzyl-2-(4-(3,5-dimethylphenyl)but-3-yn-1-yl)malononitrile (1aa):



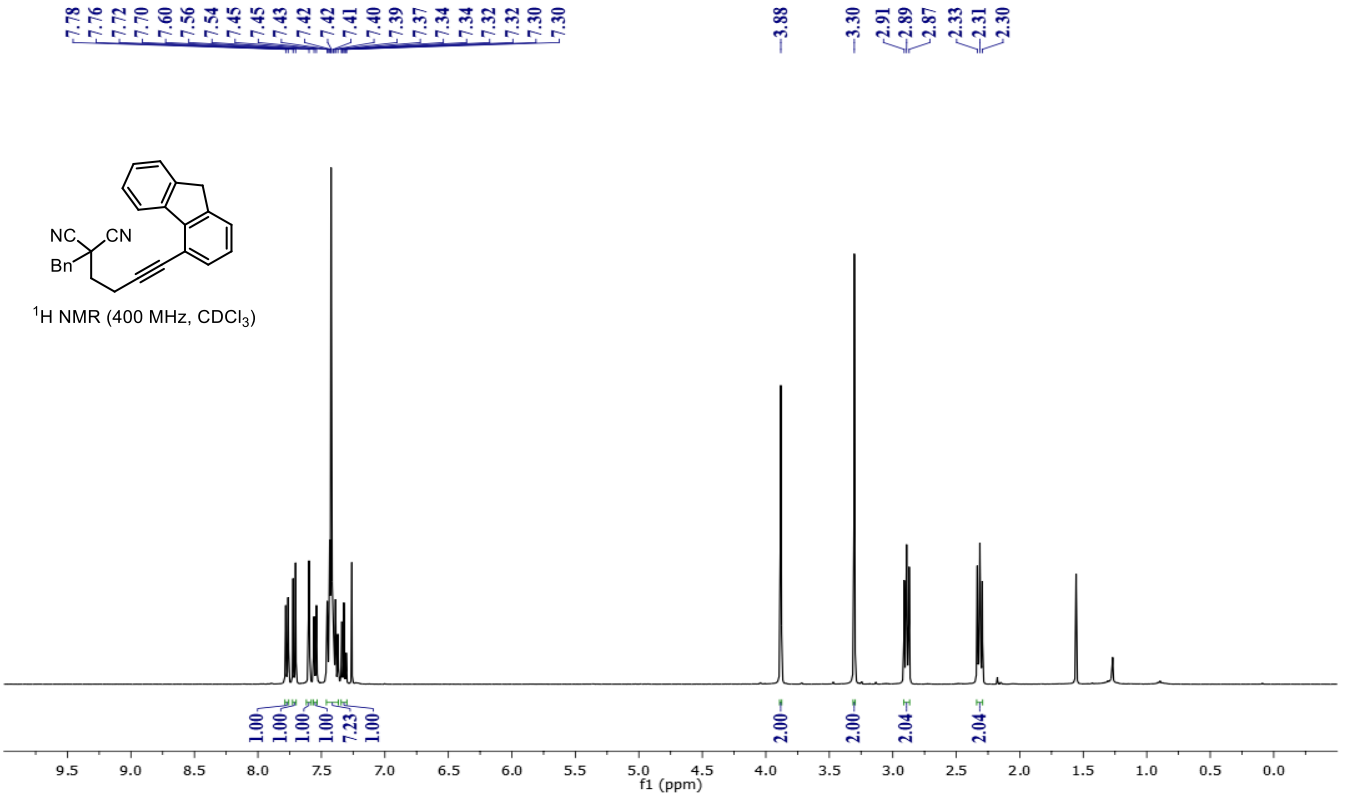


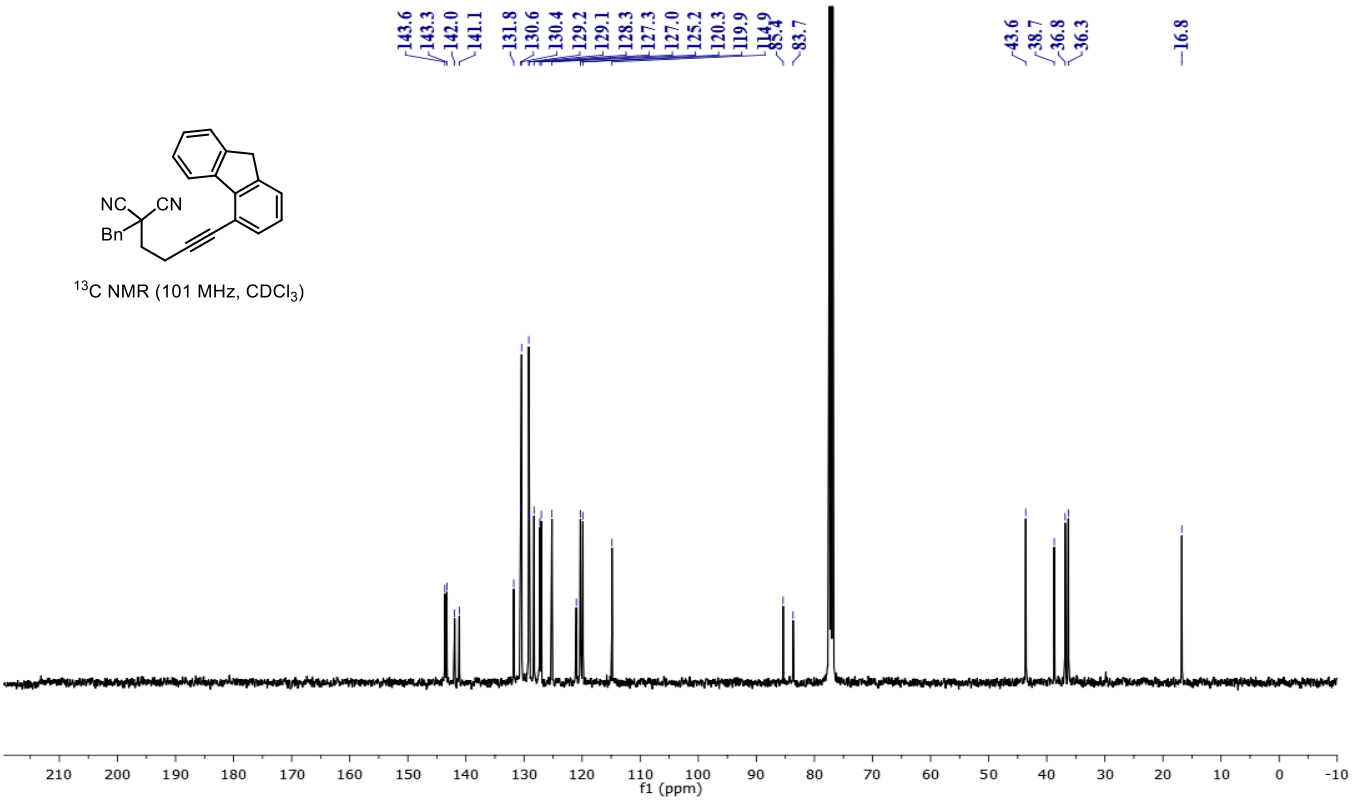
2-Benzyl-2-(4-(2,4-dimethoxyphenyl)but-3-yn-1-yl)malononitrile (1ab):



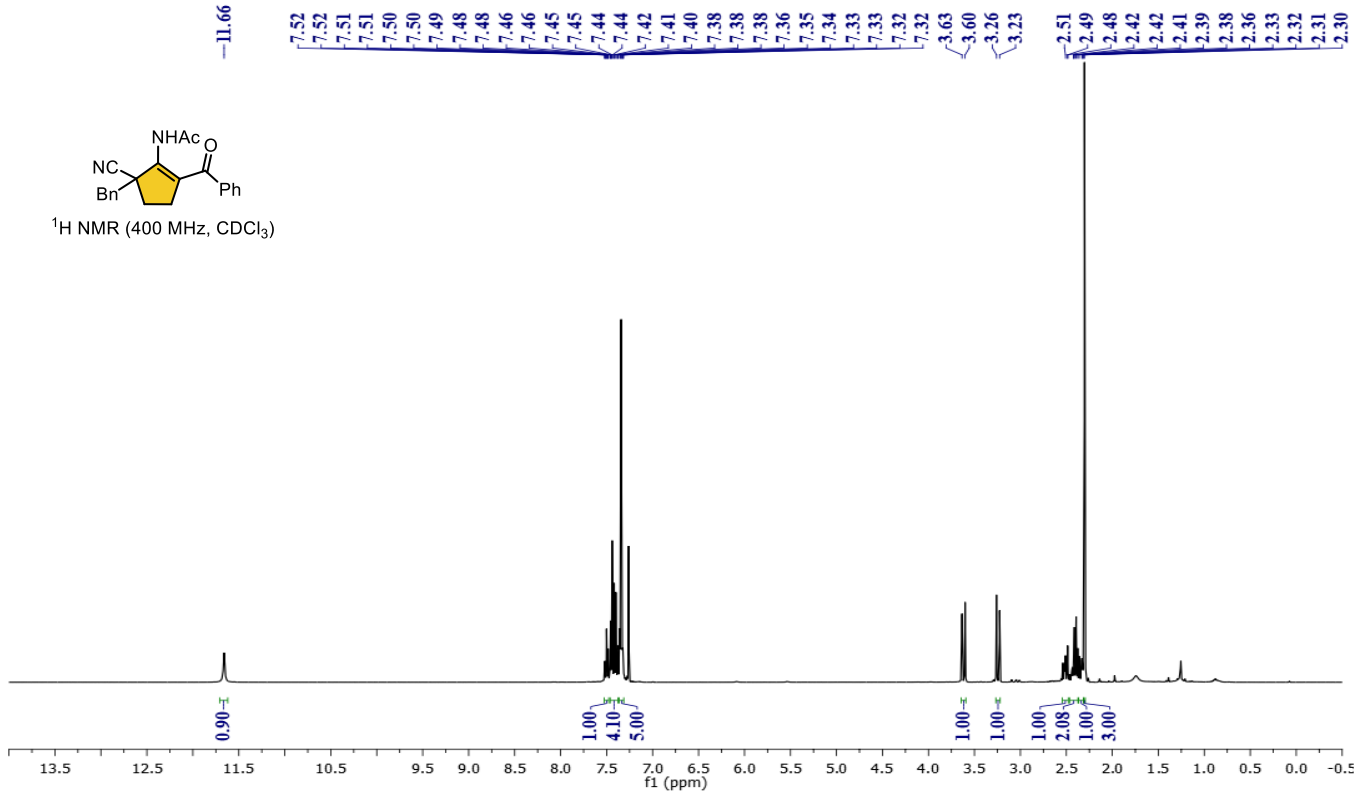


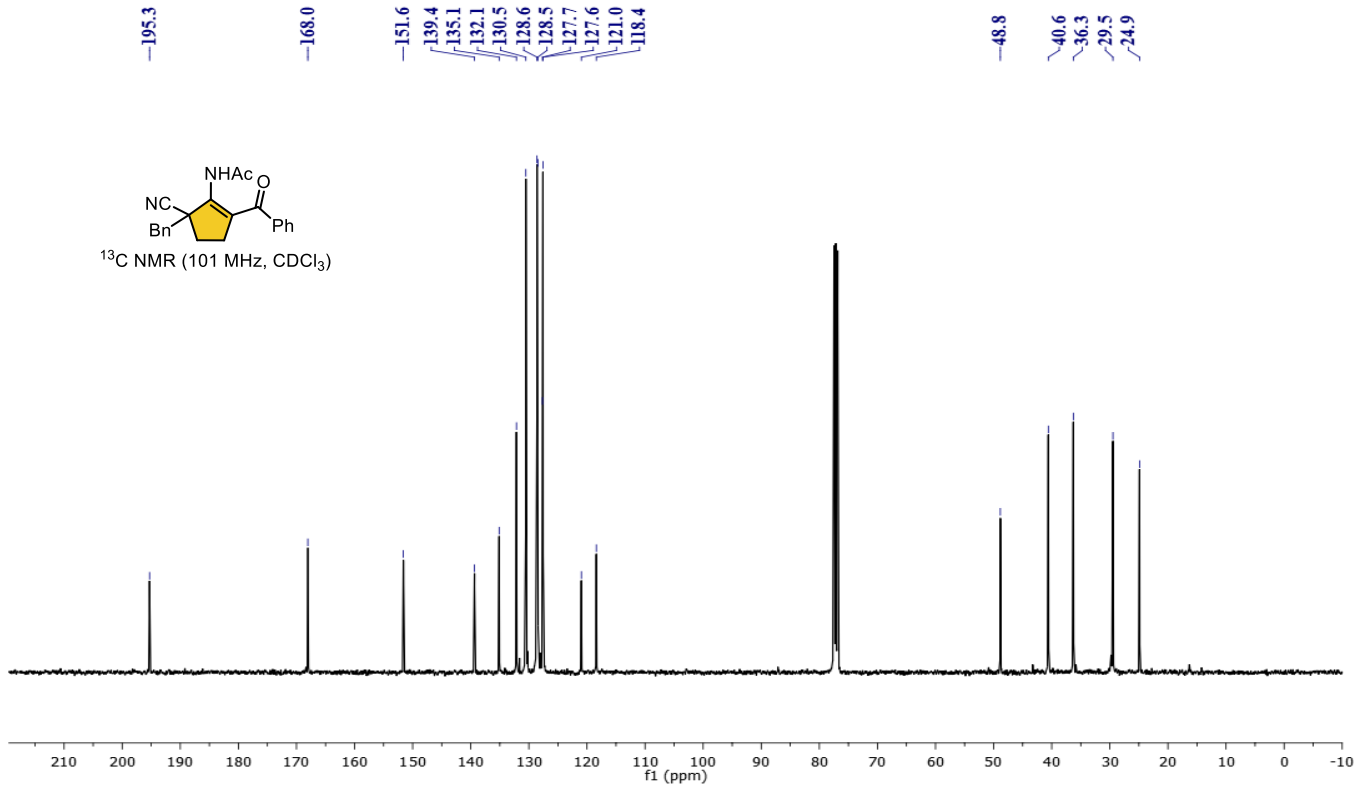
2-(4-(9*H*-Fluoren-1-yl)but-3-yn-1-yl)-2-benzylmalononitrile (1ad):



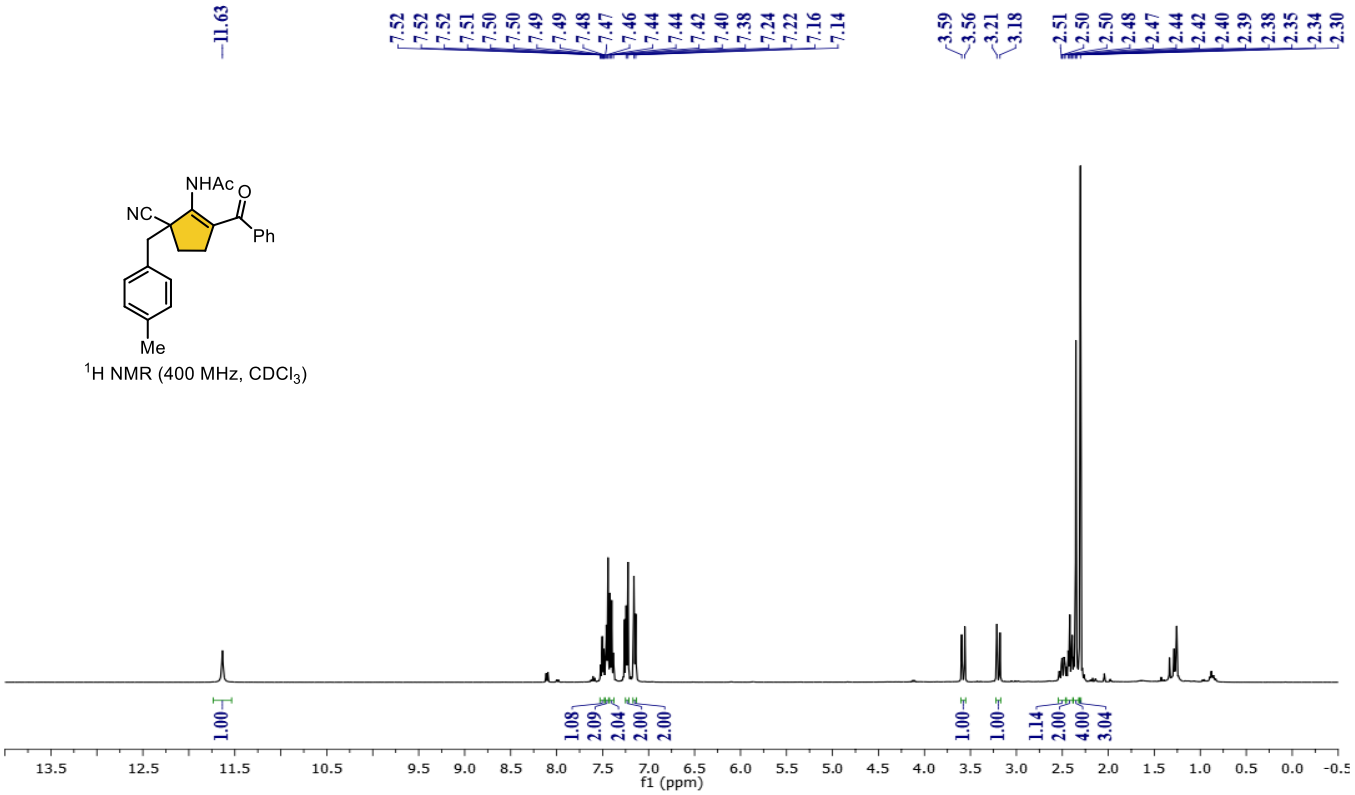


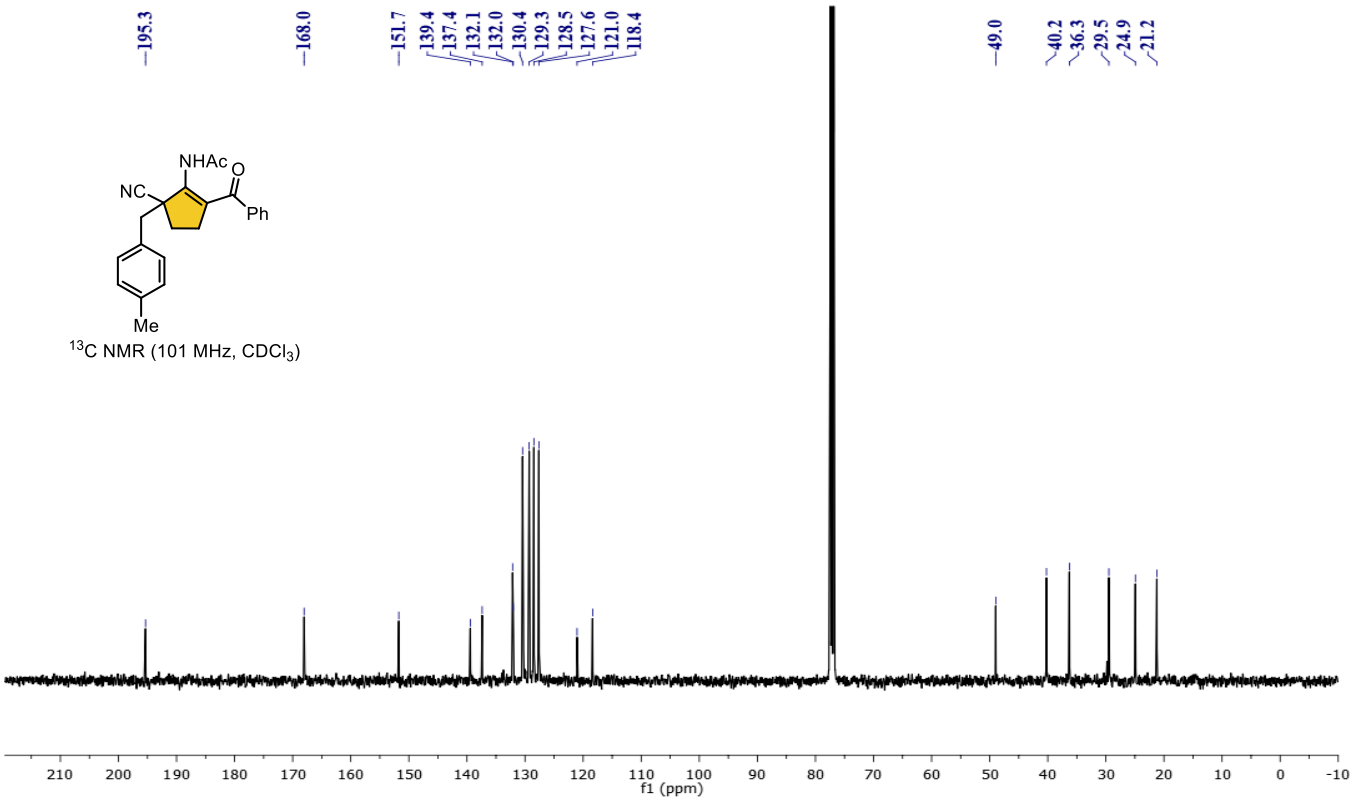
N-(2-Benzoyl-5-benzyl-5-cyanocyclopent-1-en-1-yl)acetamide (2a):



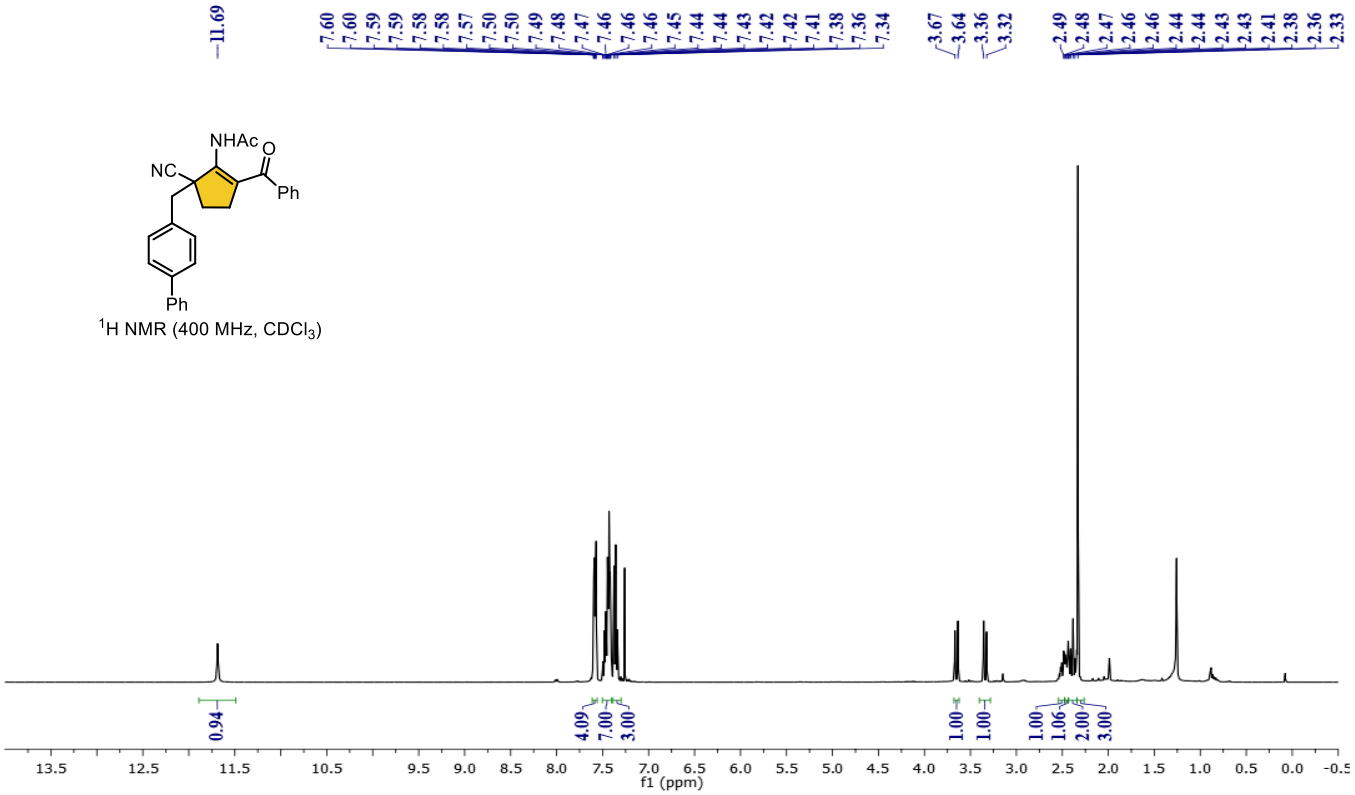


***N*-(2-benzoyl-5-cyano-5-(4-methylbenzyl)cyclopent-1-en-1-yl)acetamide (2b):**

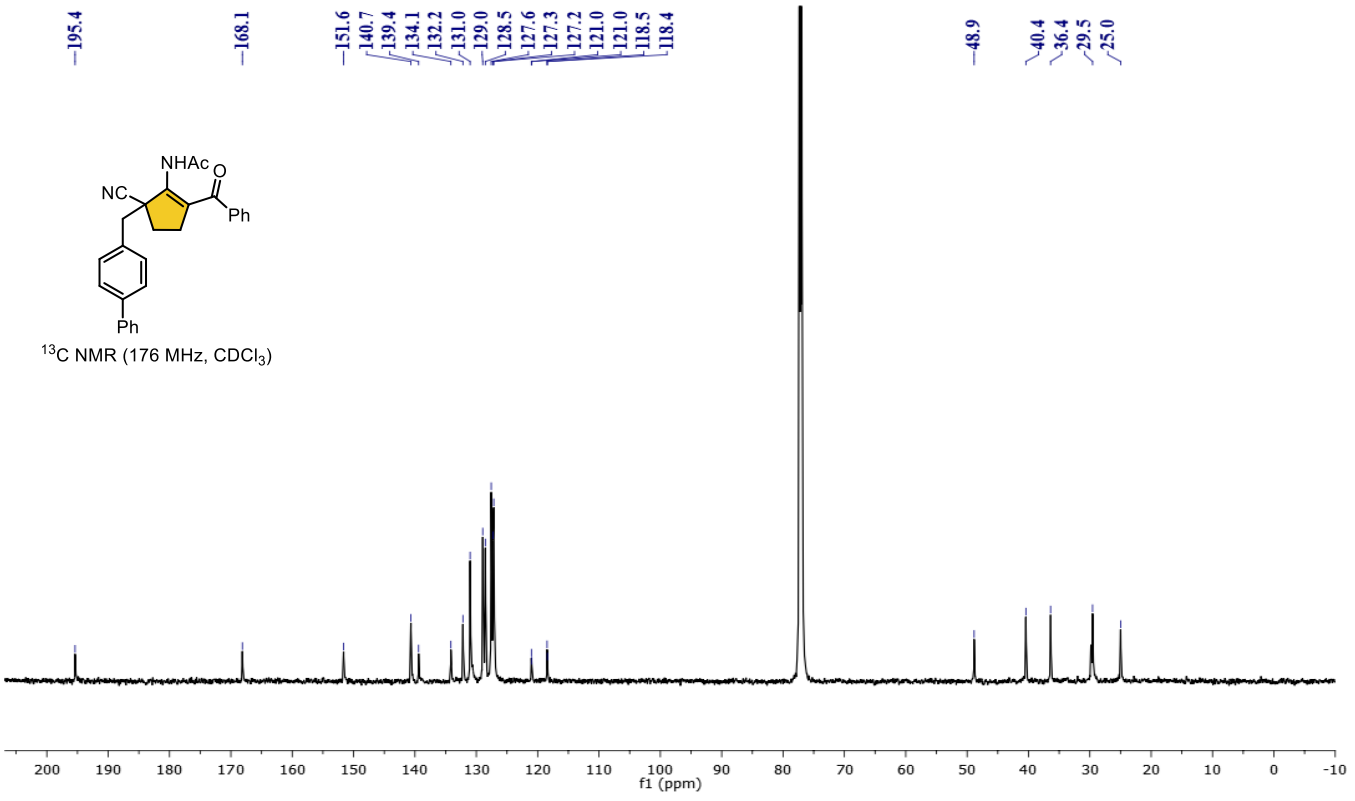




***N*-(5-([1,1'-Biphenyl]-4-ylmethyl)-2-benzoyl-5-cyanocyclopent-1-en-1-yl)acetamide (2c):**

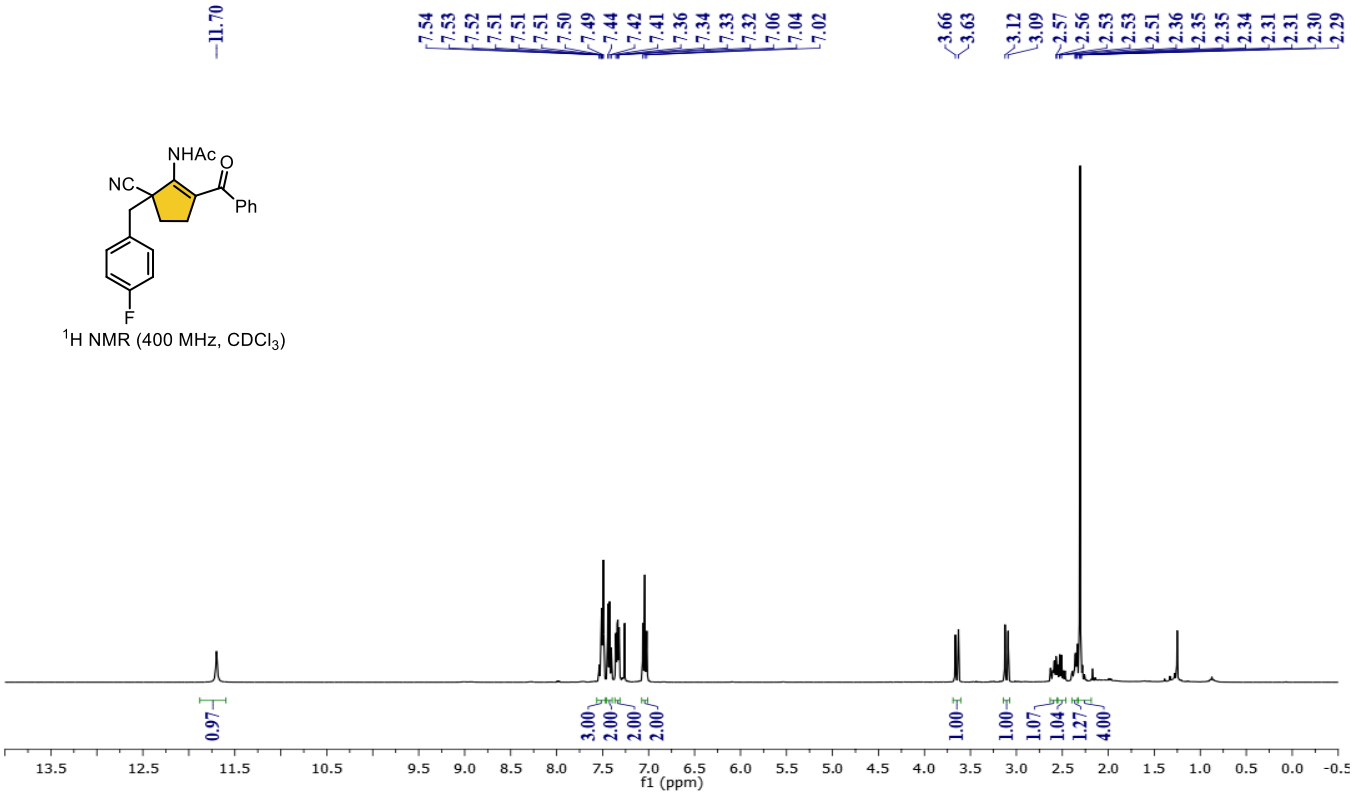


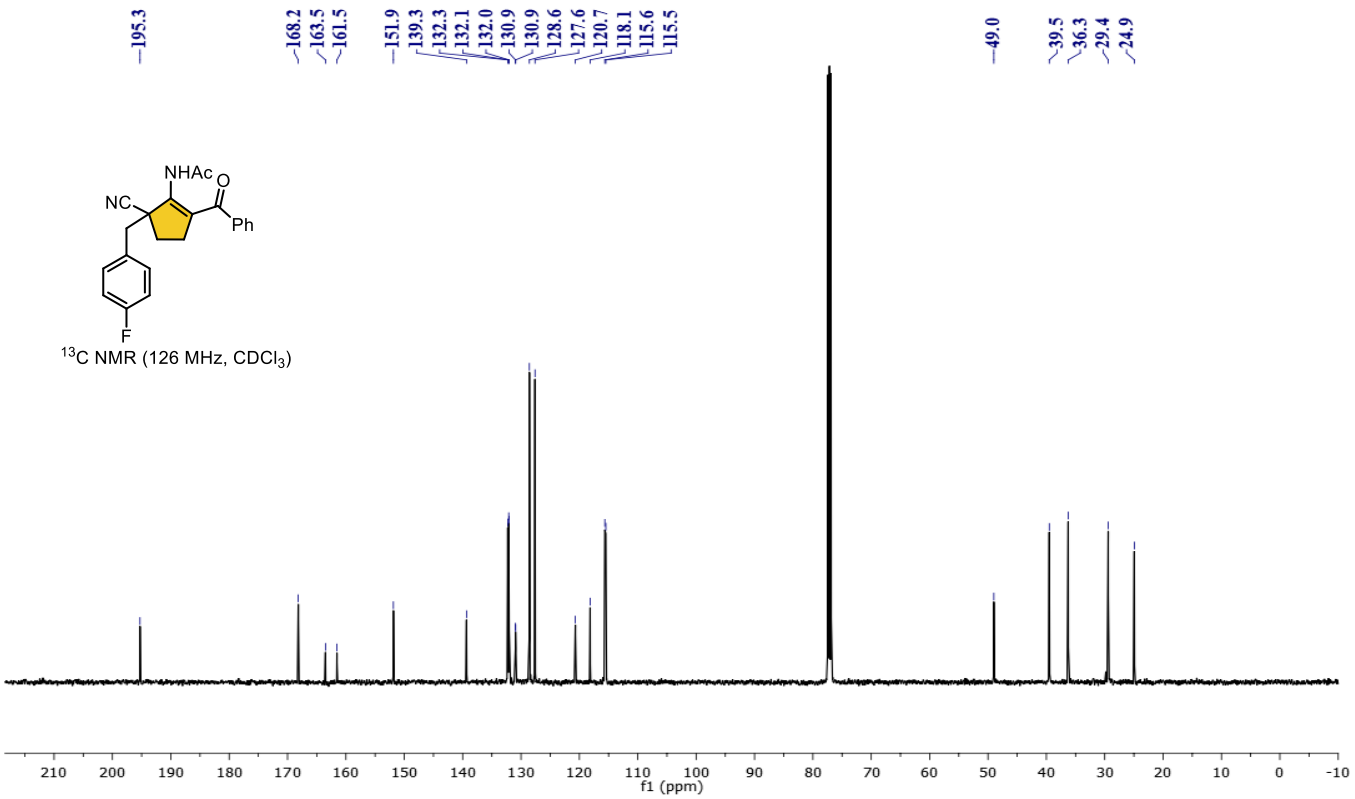
^{1}H NMR (400 MHz, $CDCl_3$)

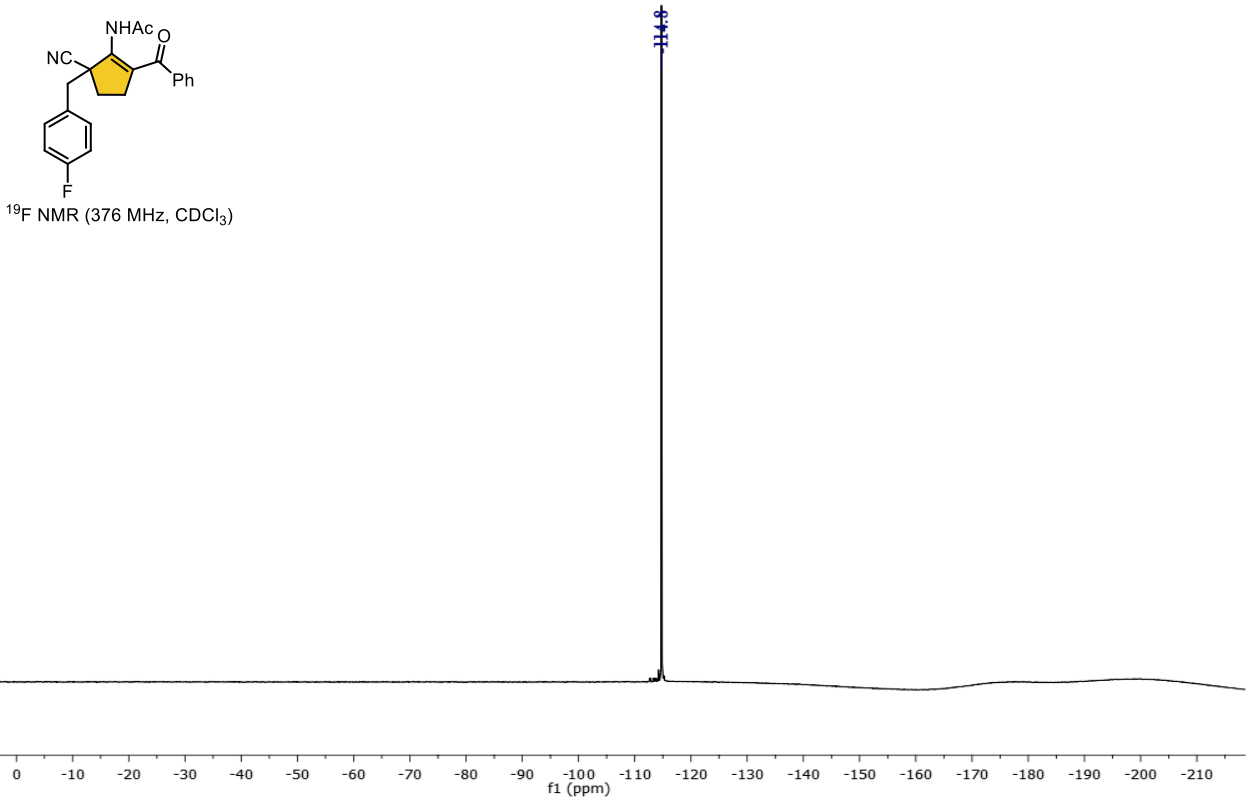


^{13}C NMR (176 MHz, $CDCl_3$)

***N*-(2-Benzoyl-5-cyano-5-(4-fluorobenzyl)cyclopent-1-en-1-yl)acetamide (2d):**

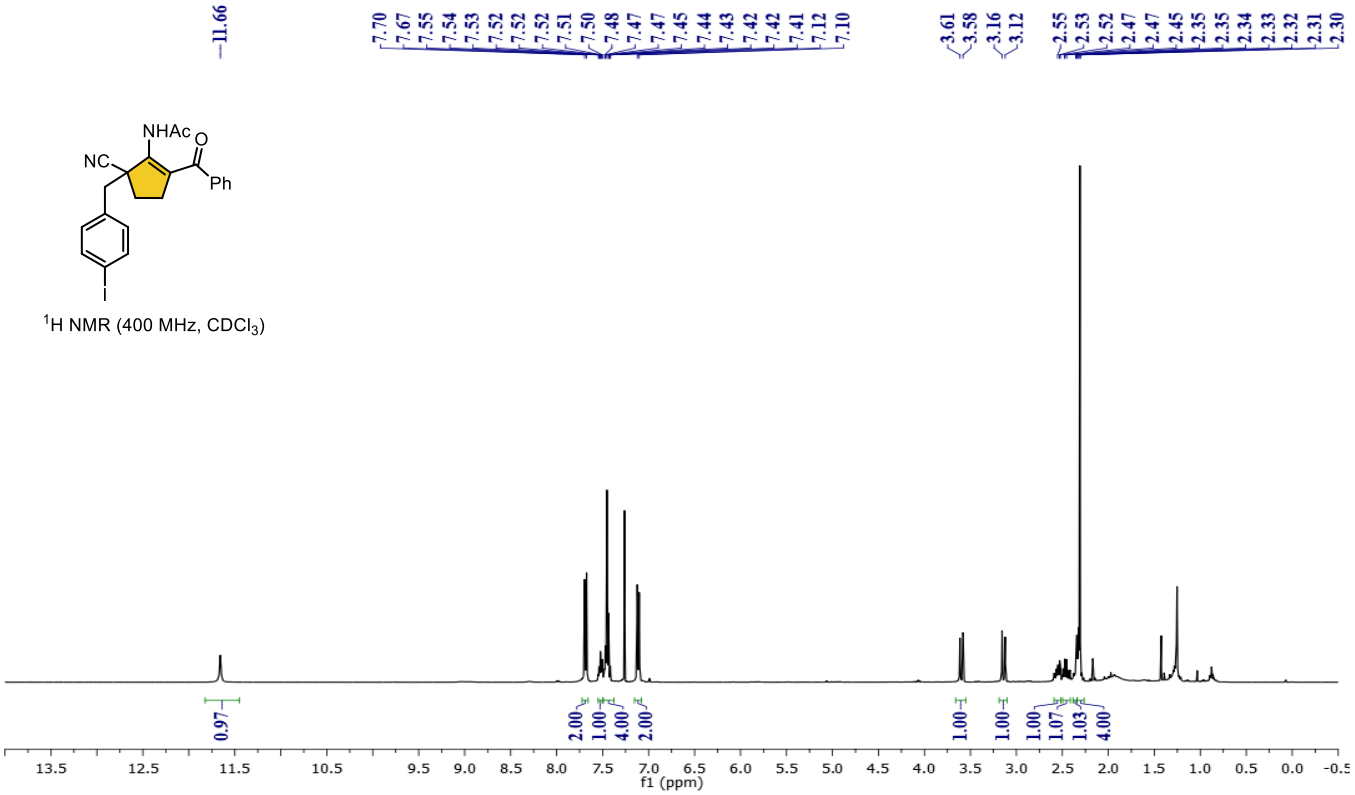




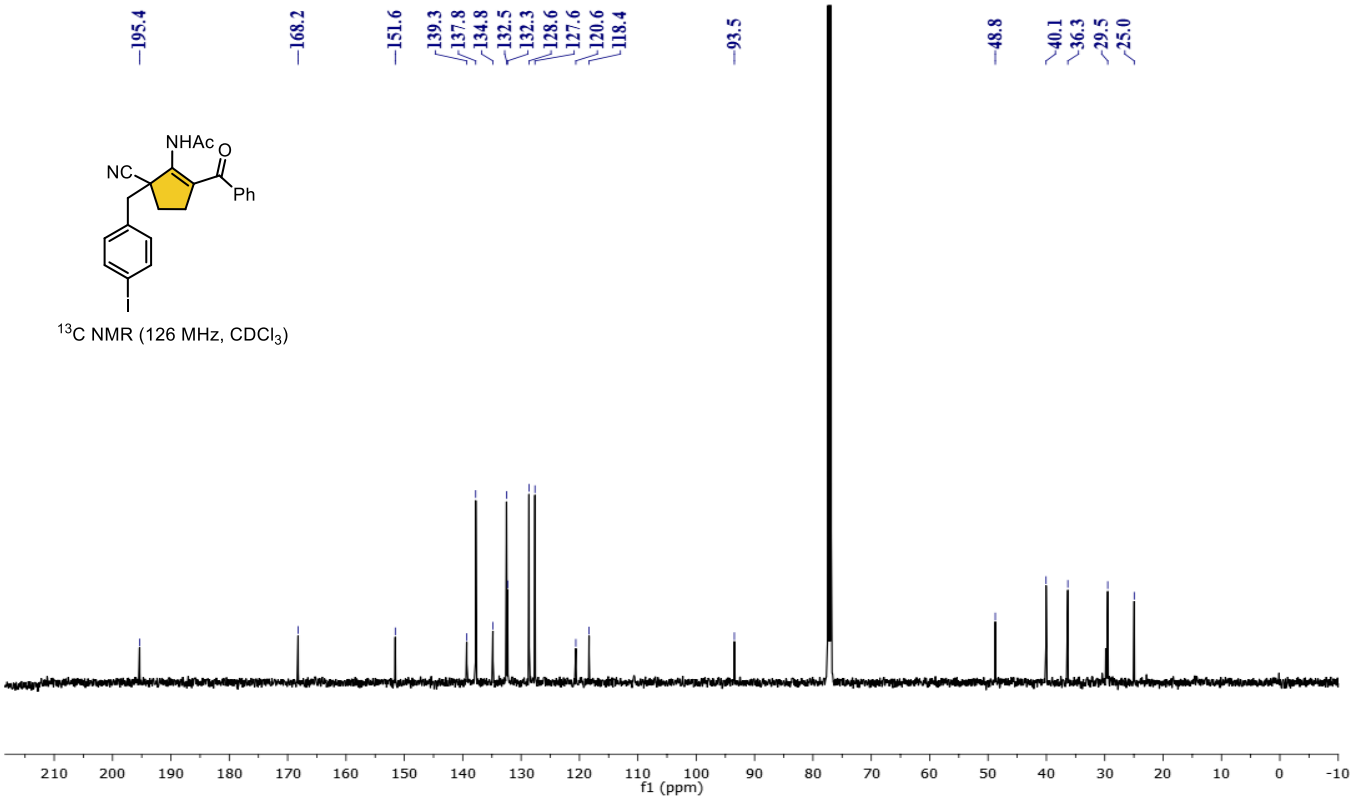


^{19}F NMR (376 MHz, $CDCl_3$)

***N*-(2-Benzoyl-5-cyano-5-(4-iodobenzyl)cyclopent-1-en-1-yl)acetamide (2e):**

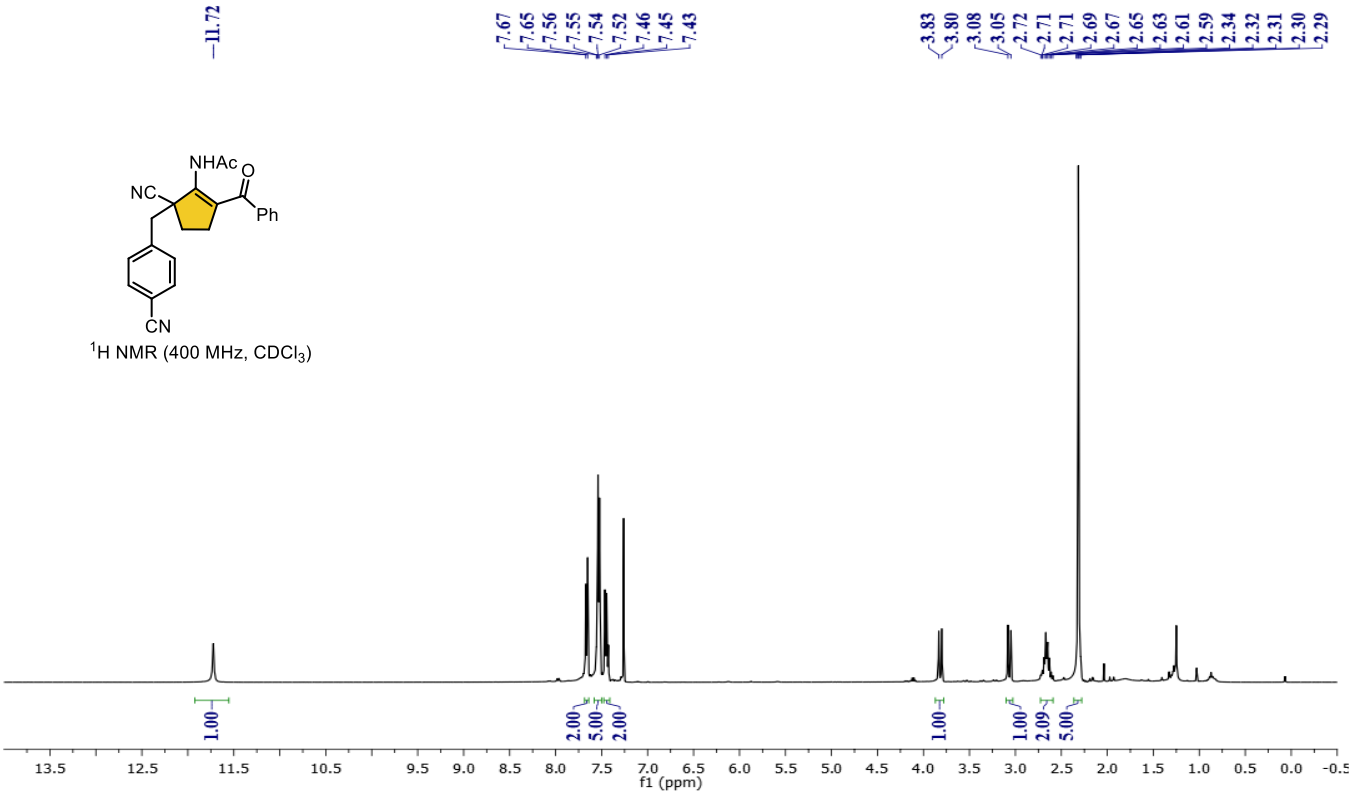


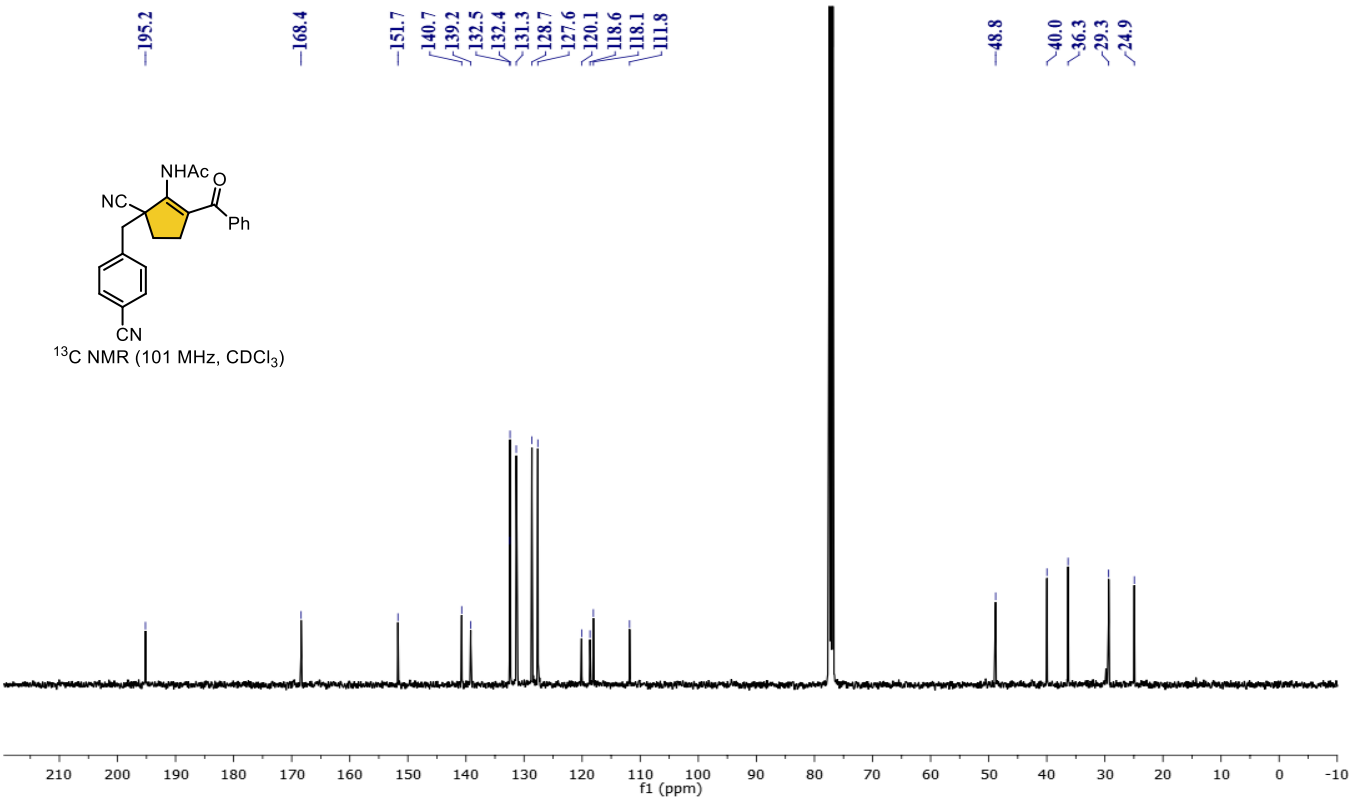
^{1}H NMR (400 MHz, $CDCl_3$)



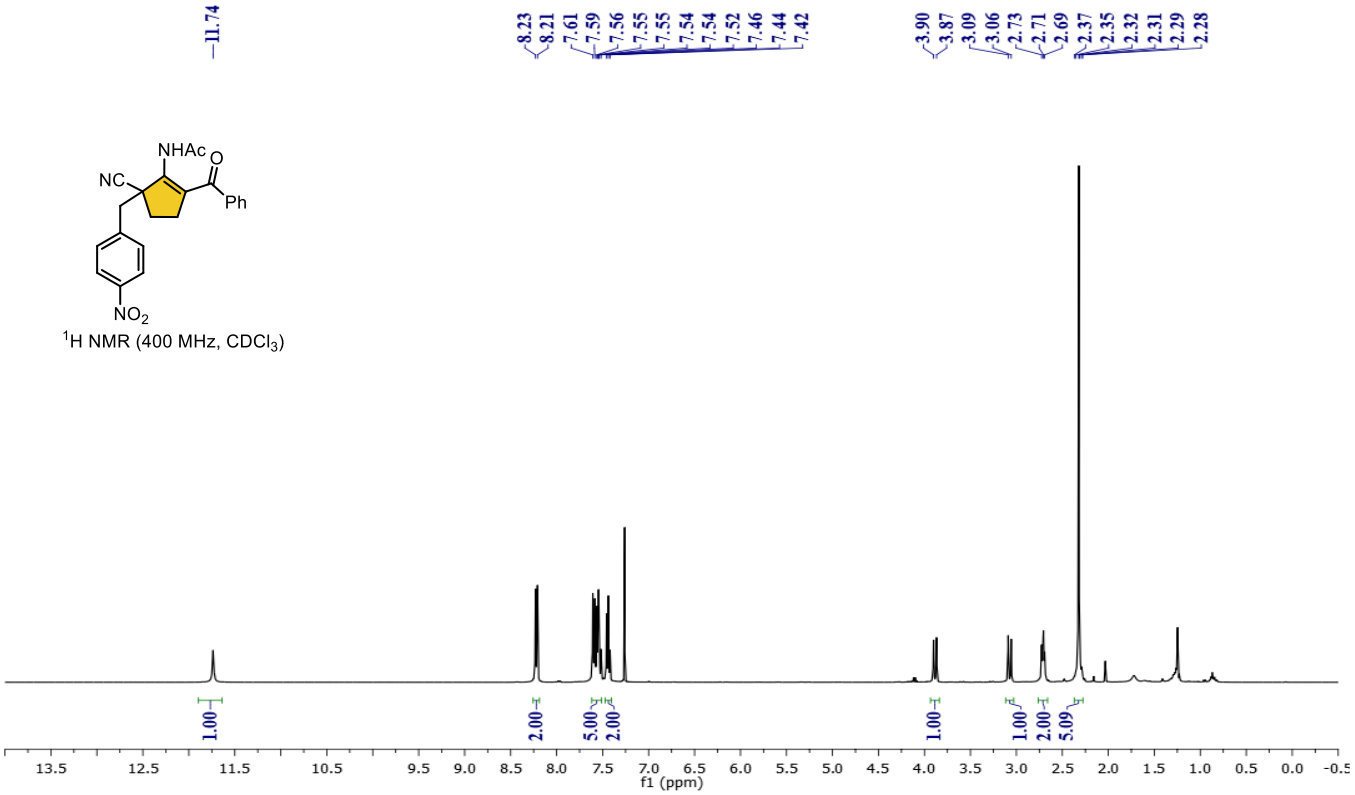
^{13}C NMR (126 MHz, $CDCl_3$)

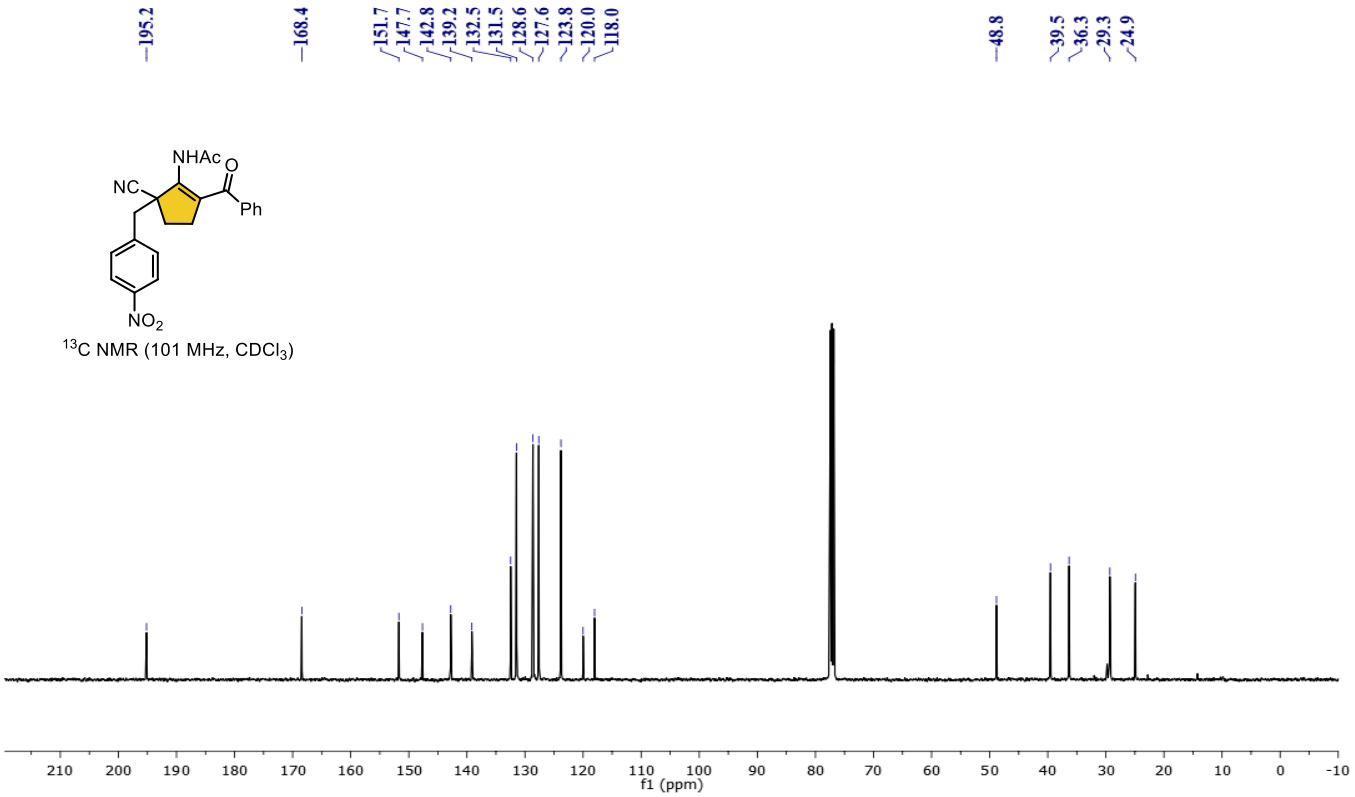
***N*-(2-Benzoyl-5-cyano-5-(4-cyanobenzyl)cyclopent-1-en-1-yl)acetamide (2f):**



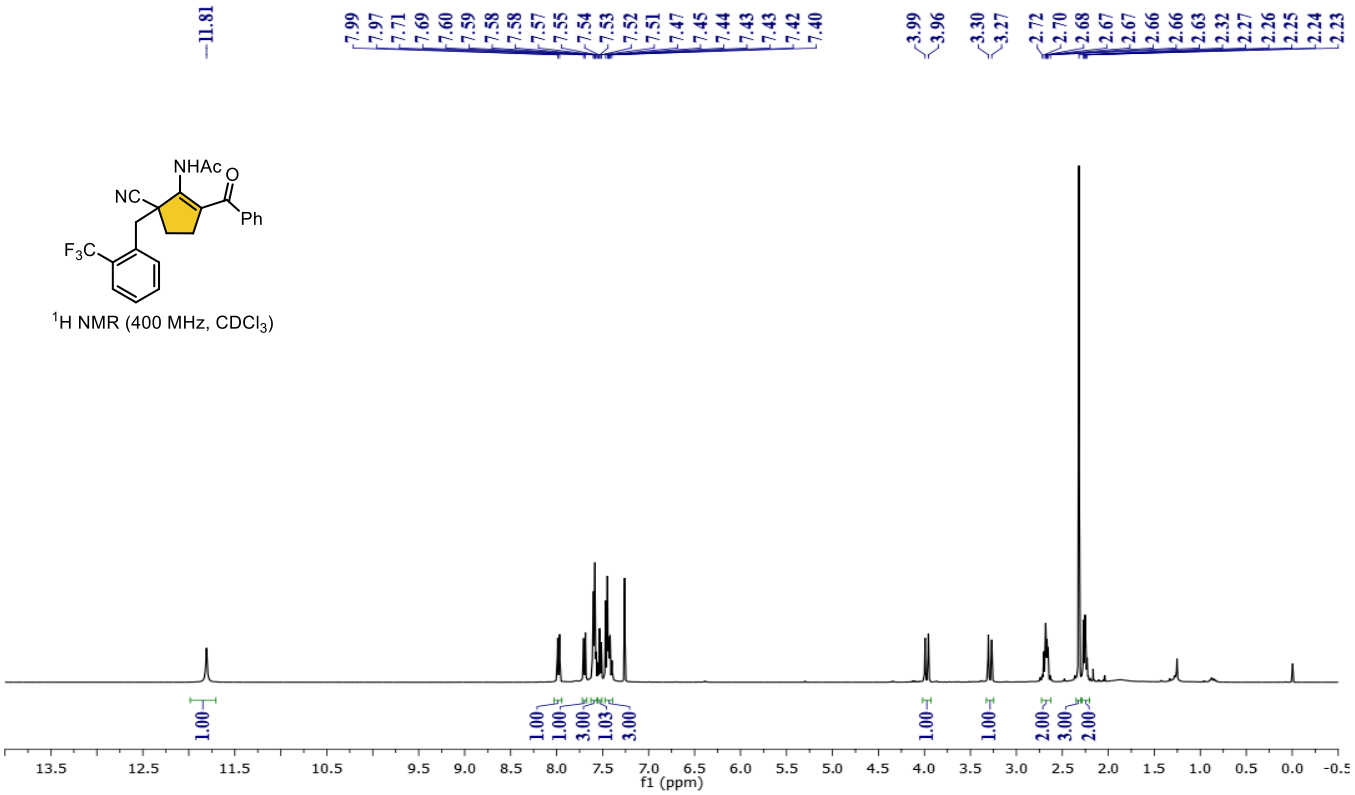


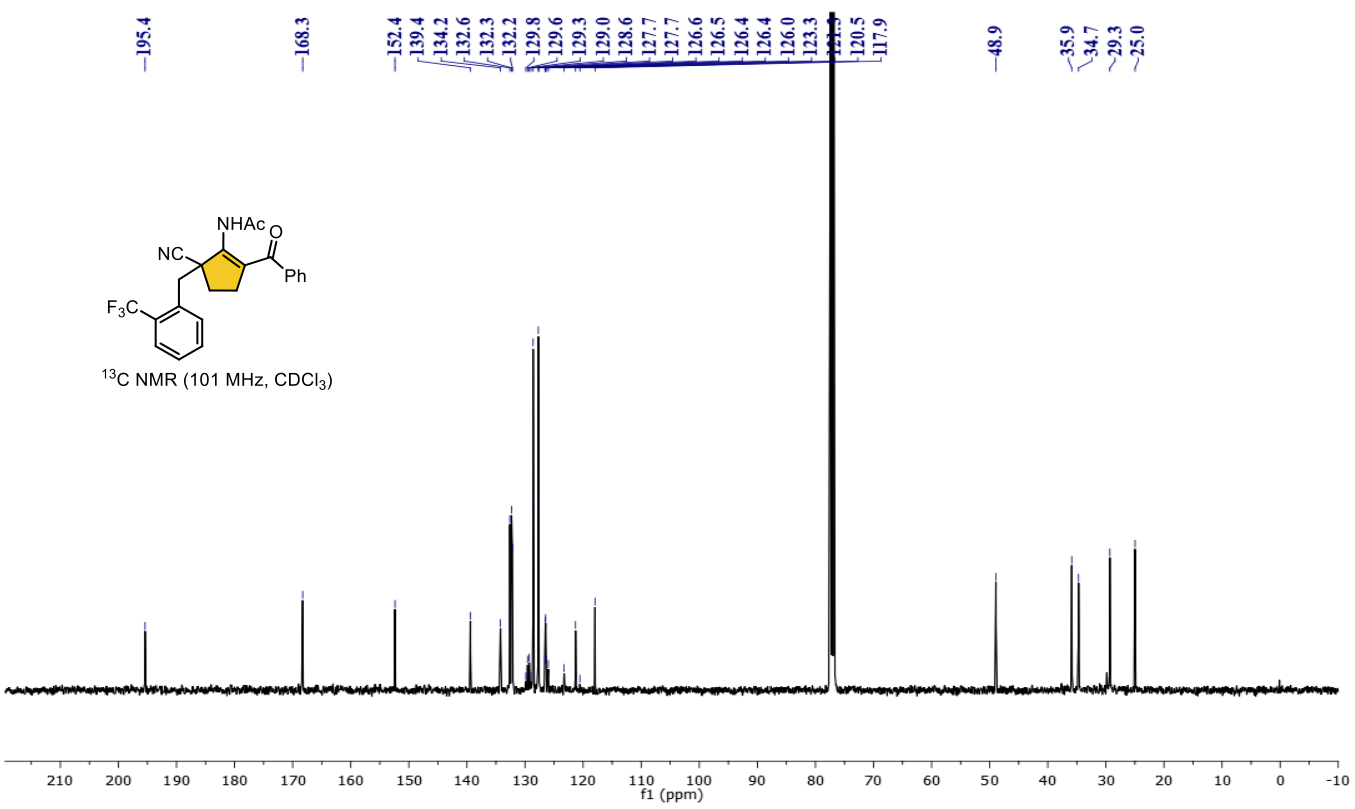
_N_-(2-Benzoyl-5-cyano-5-(4-nitrobenzyl)cyclopent-1-en-1-yl)acetamide (2g):

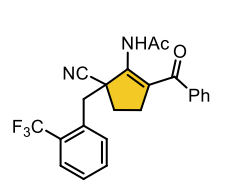




_N_-(2-Benzoyl-5-cyano-5-(2-(trifluoromethyl)benzyl)cyclopent-1-en-1-yl)acetamide (2h):

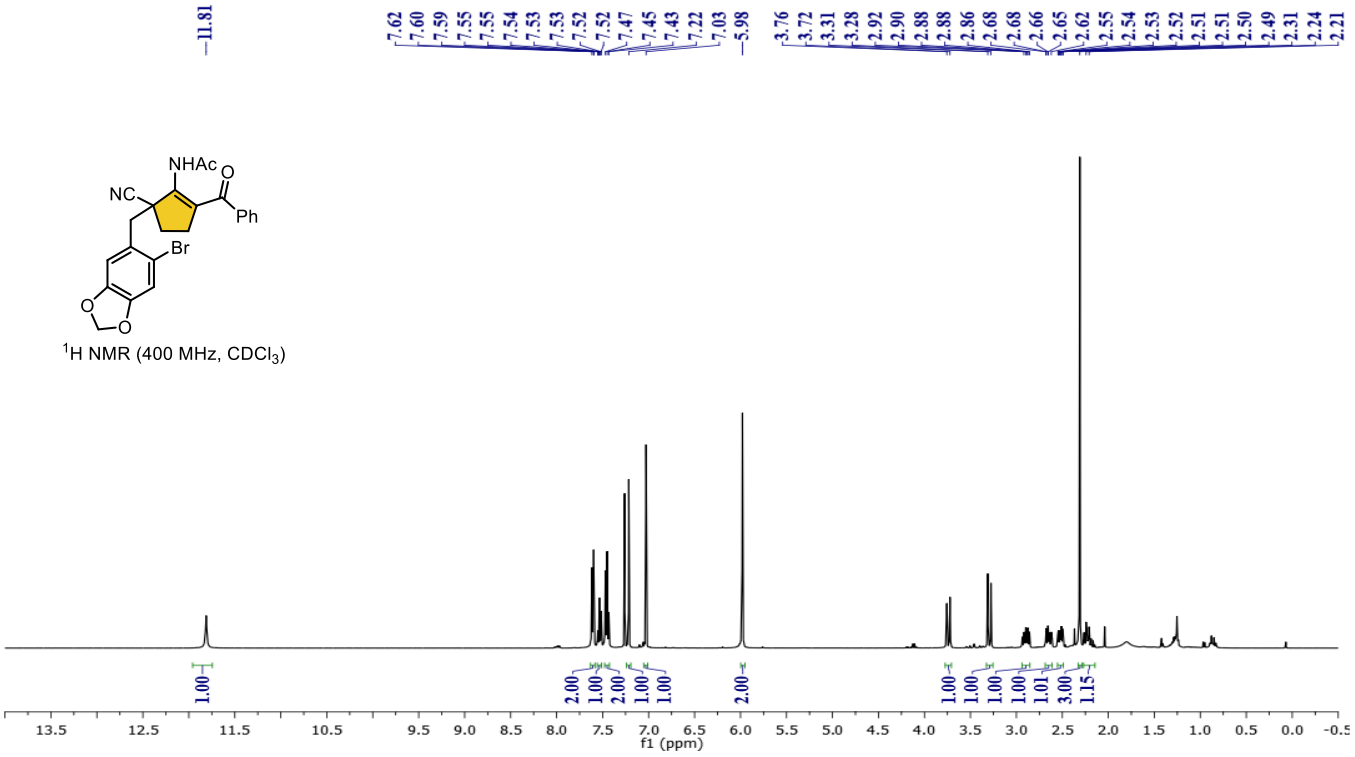


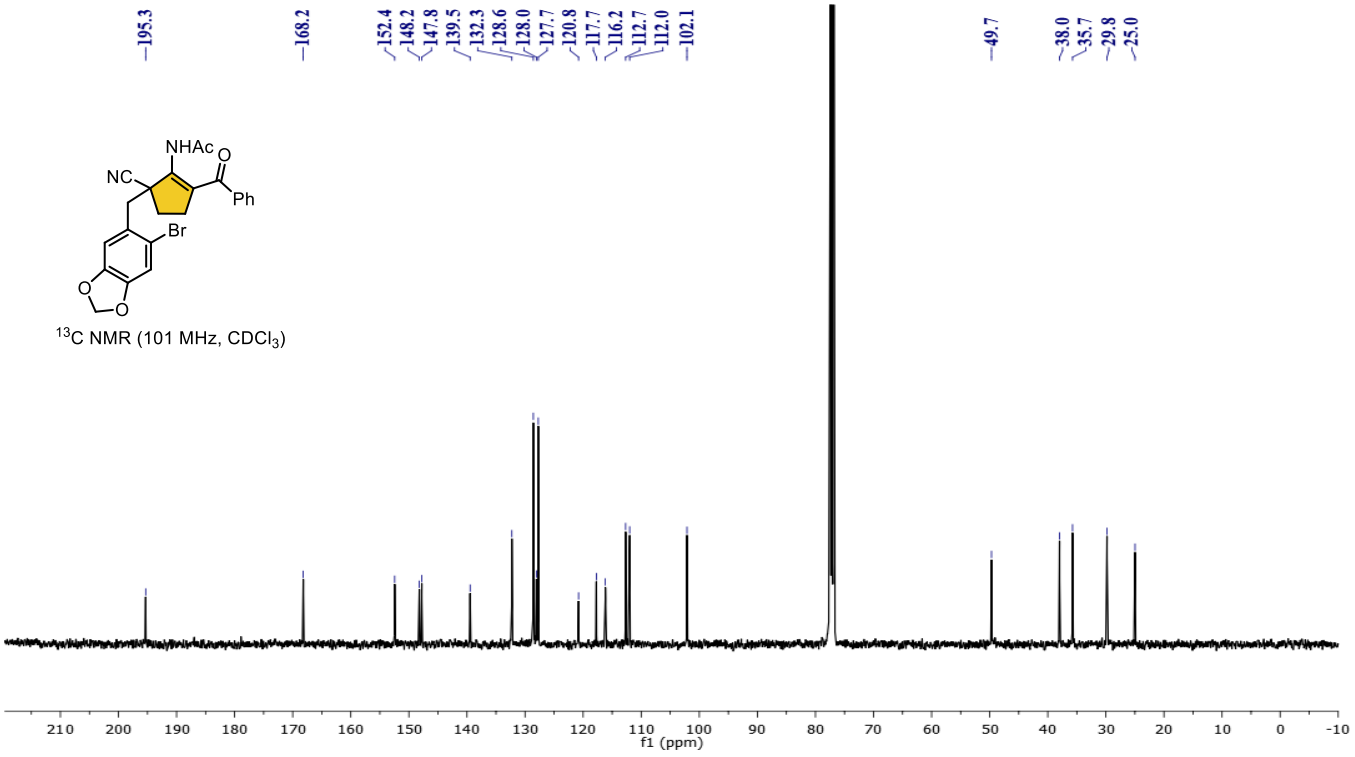




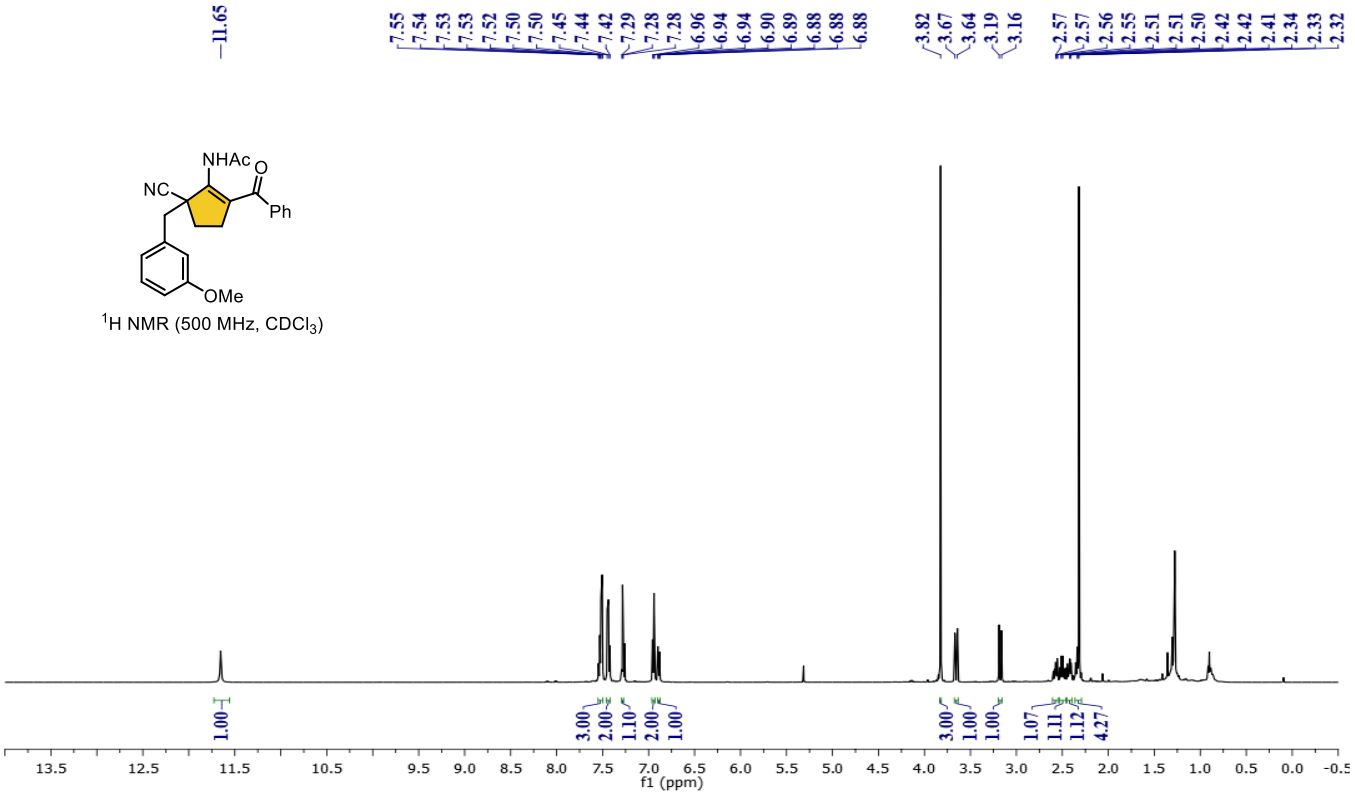
^{19}F NMR (376 MHz, $CDCl_3$)

_N_-(2-Benzoyl-5-((6-bromobenzo[_d_][1,3]dioxol-5-yl)methyl)-5-cyanocyclopent-1-en-1-yl)acetamide (2i):

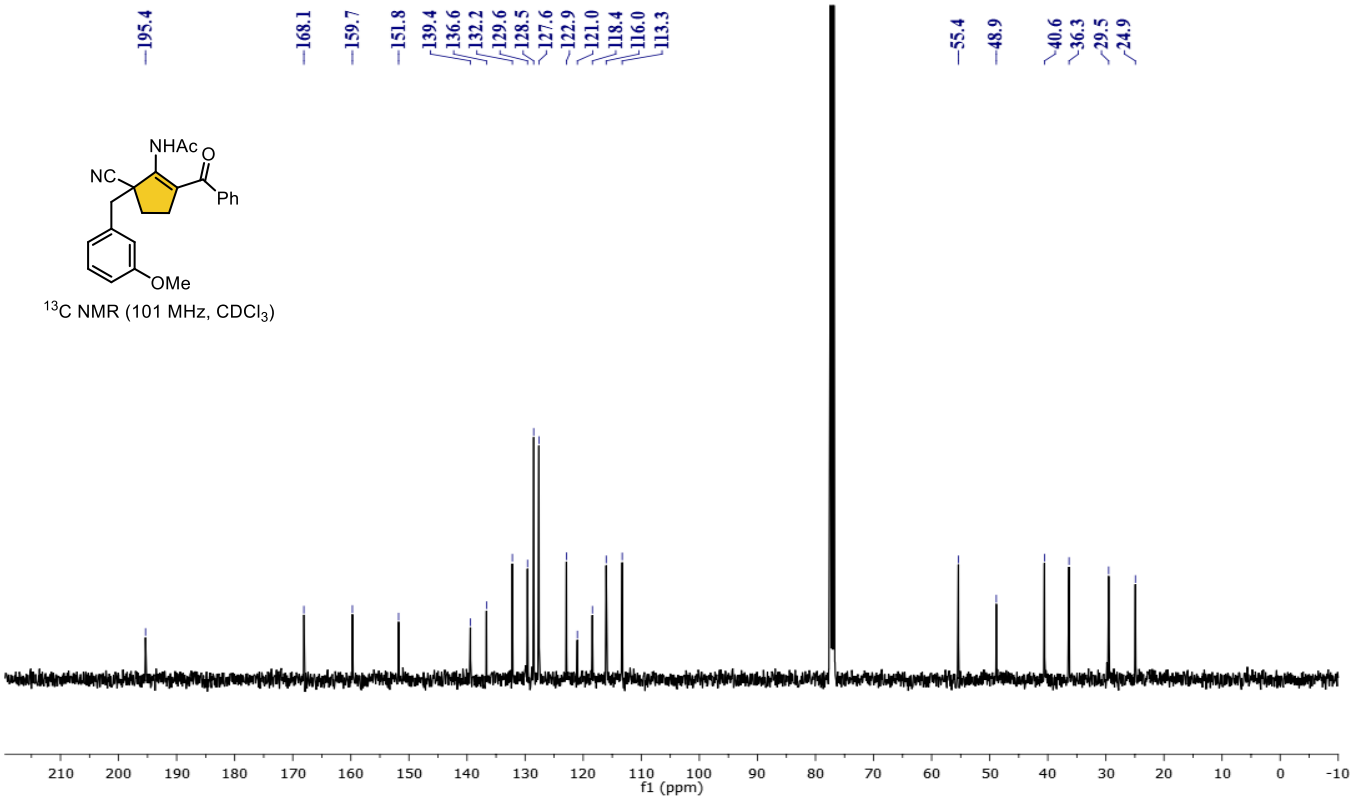




***N*-(2-Benzoyl-5-cyano-5-(3-methoxybenzyl)cyclopent-1-en-1-yl)acetamide (2j):**

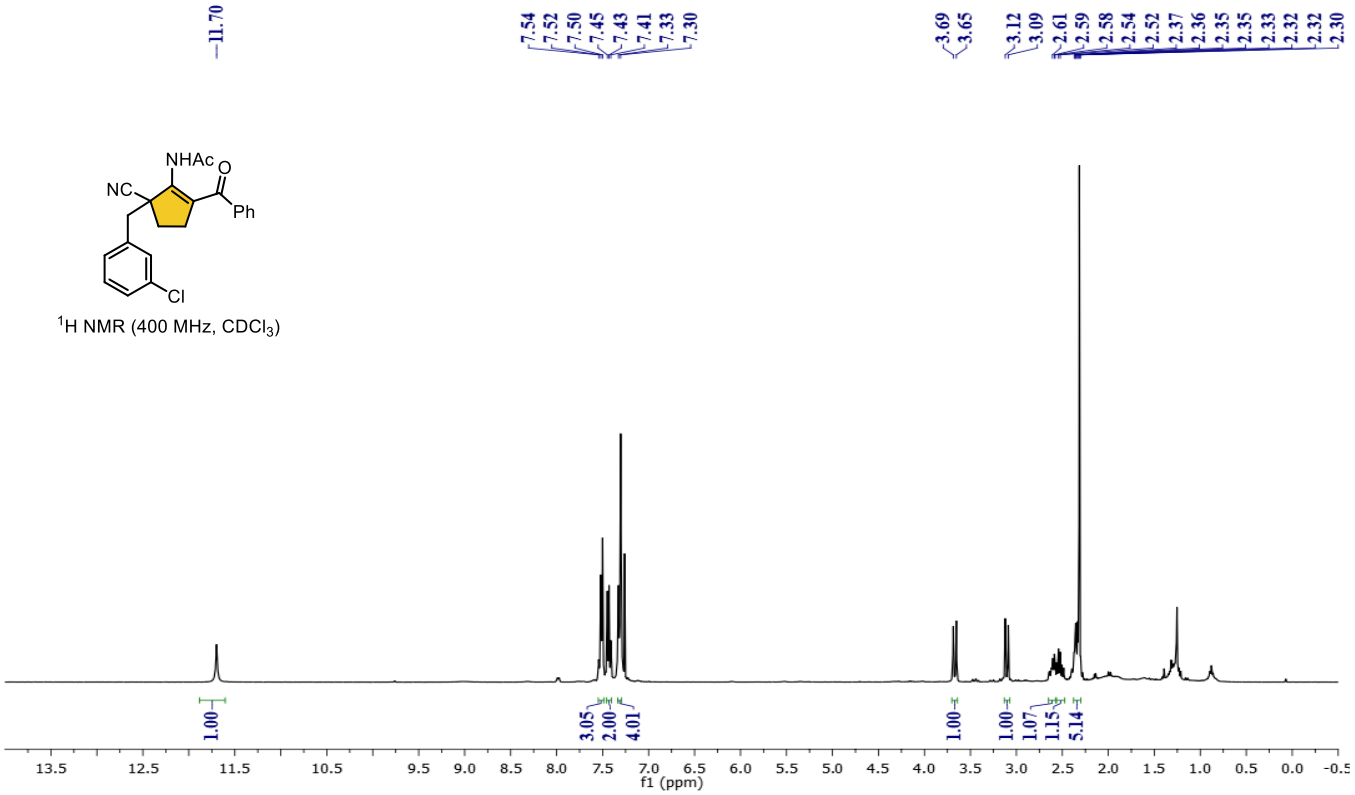


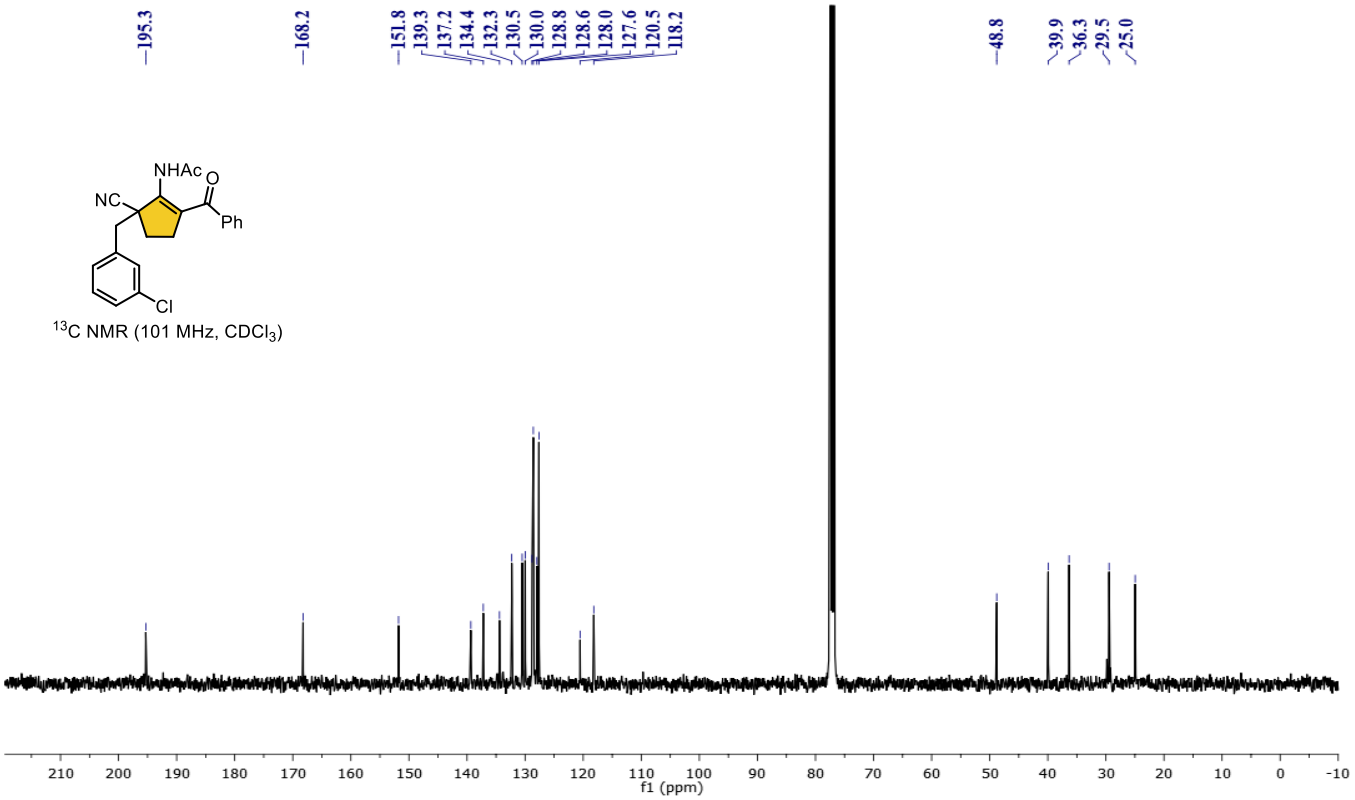
^{1}H NMR (500 MHz, $CDCl_3$)



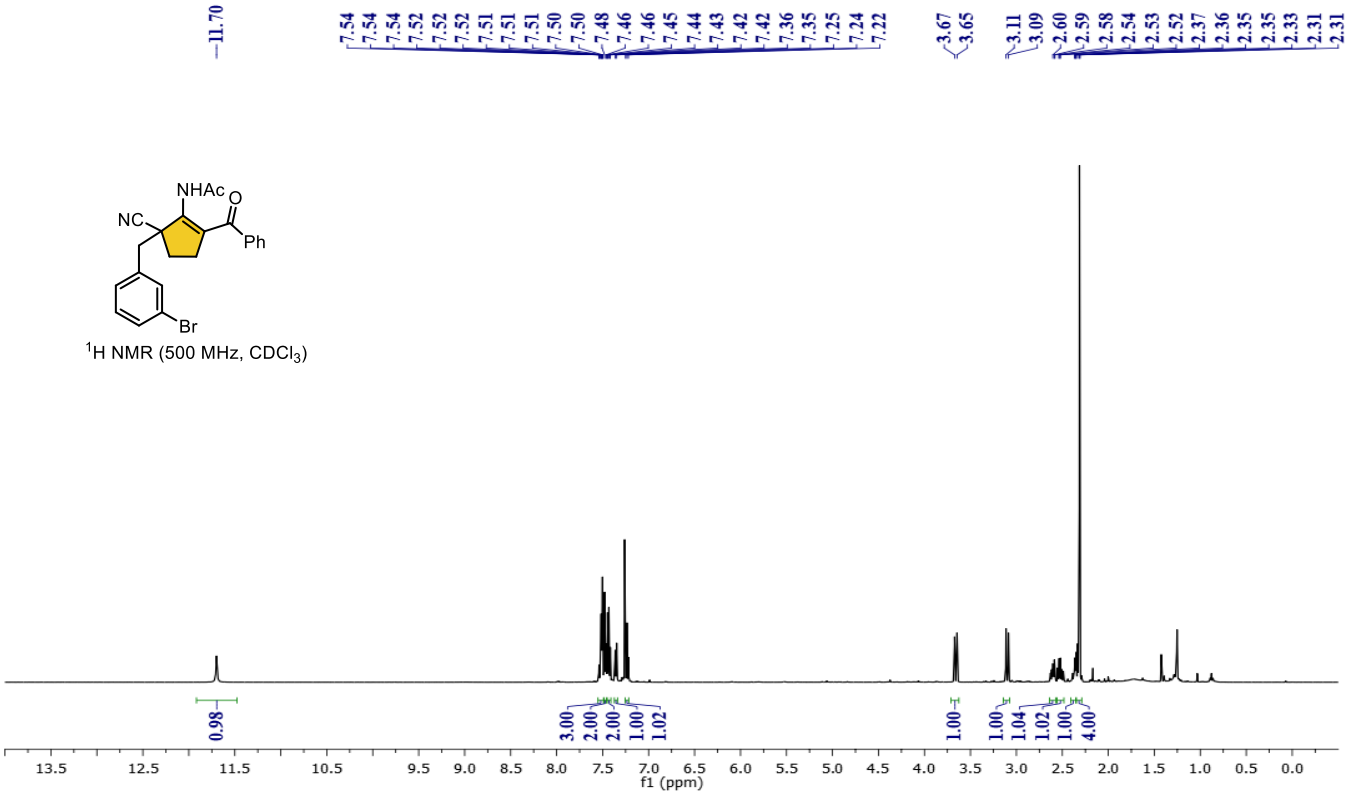
^{13}C NMR (101 MHz, $CDCl_3$)

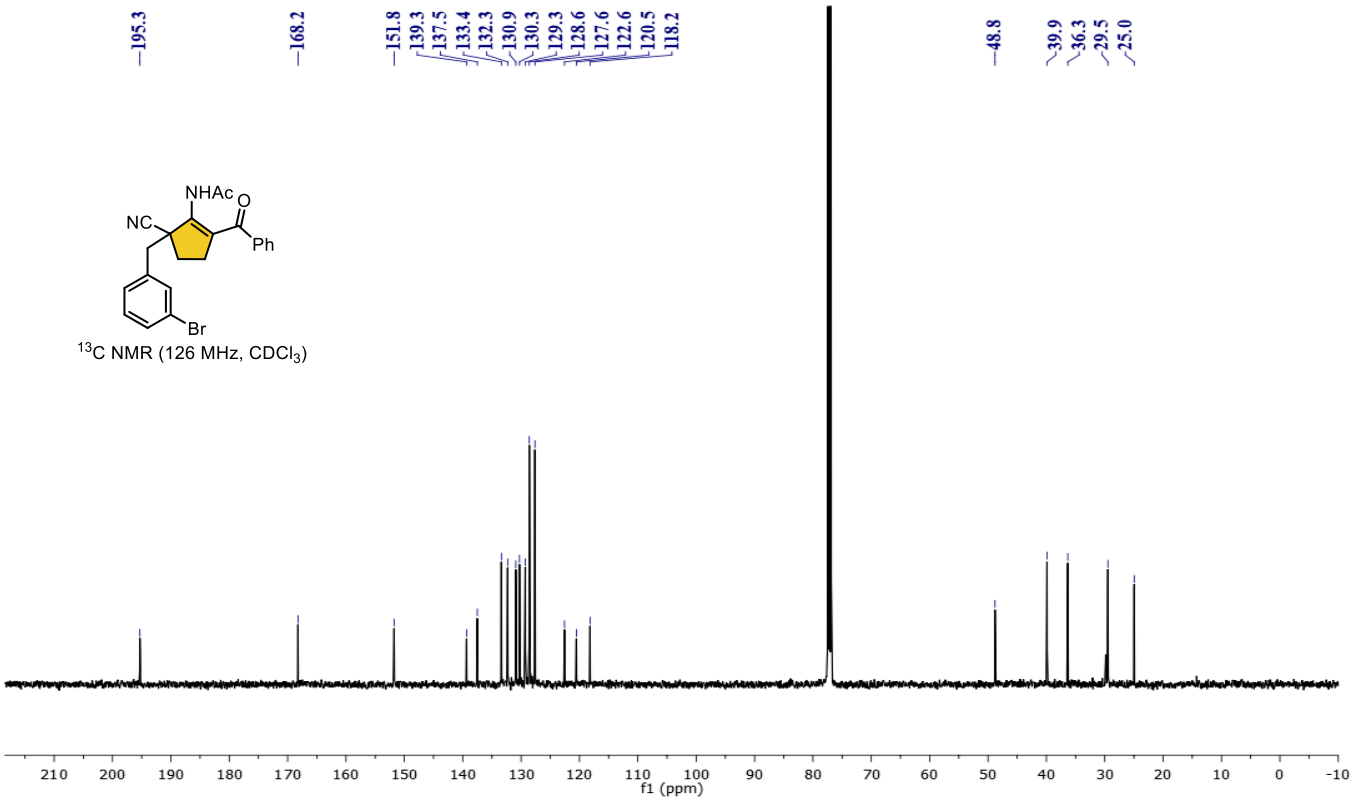
_N_-(2-Benzoyl-5-(3-chlorobenzyl)-5-cyanocyclopent-1-en-1-yl)acetamide (2k):



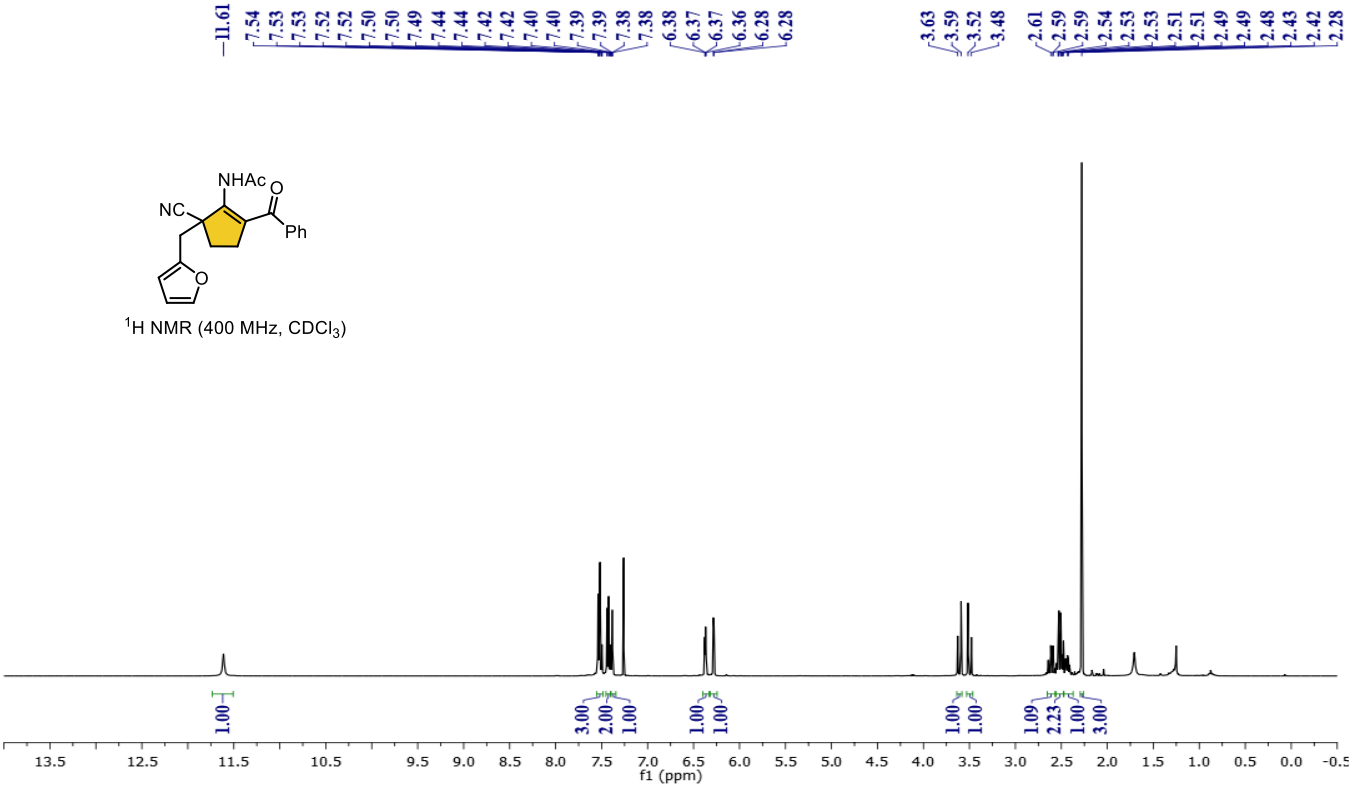


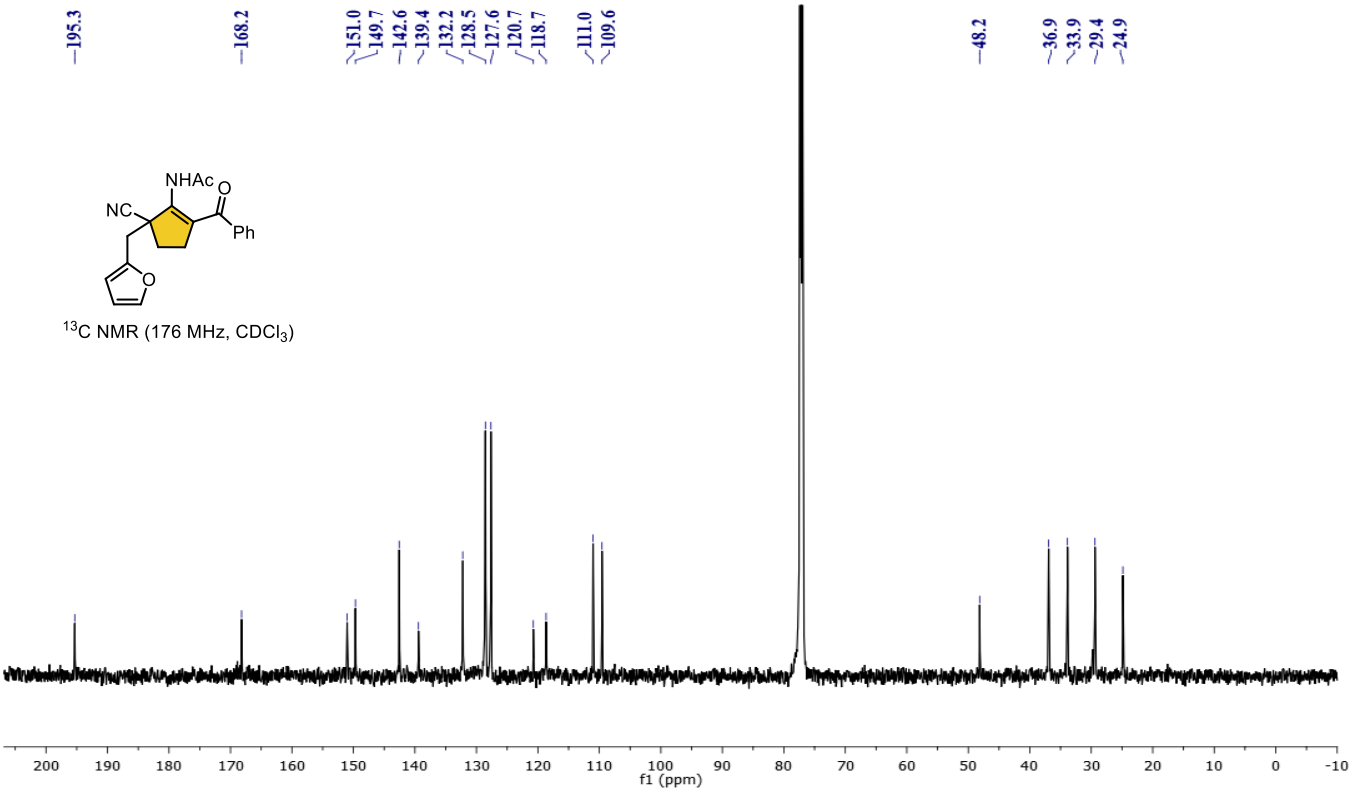
_N_-(2-Benzoyl-5-(3-bromobenzyl)-5-cyanocyclopent-1-en-1-yl)acetamide (2l):



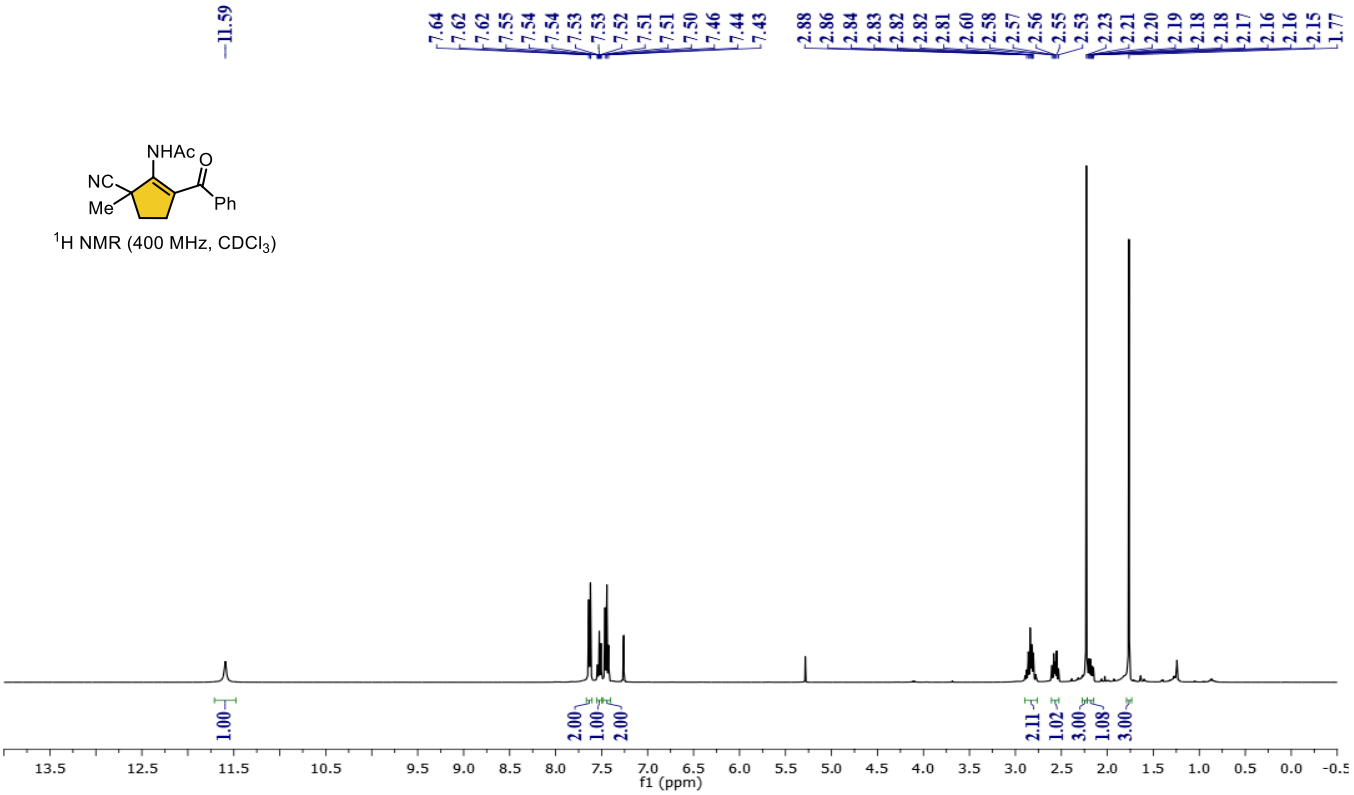


***N*-(2-Benzoyl-5-cyano-5-(furan-2-ylmethyl)cyclopent-1-en-1-yl)acetamide (2m):**

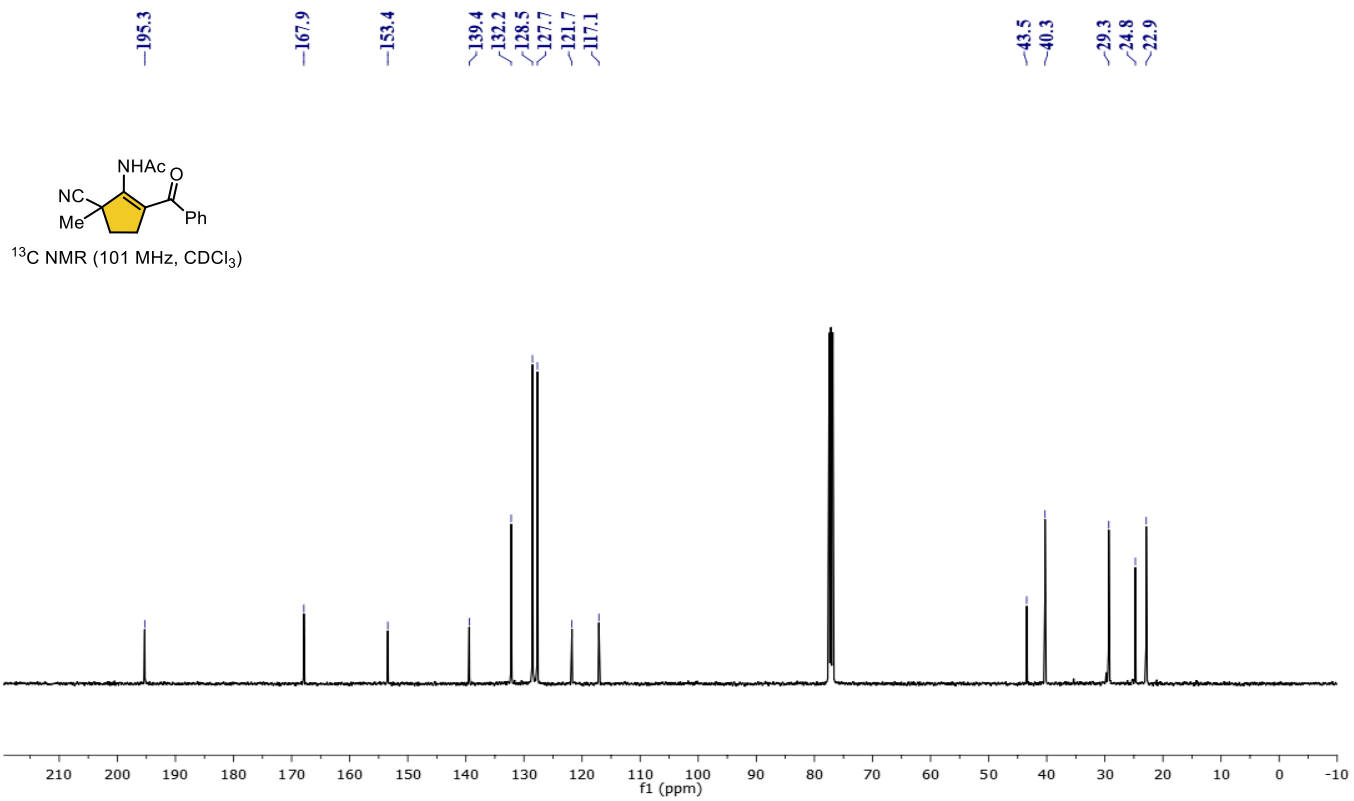




N-(2-benzoyl-5-cyano-5-methylcyclopent-1-en-1-yl)acetamide (2n):

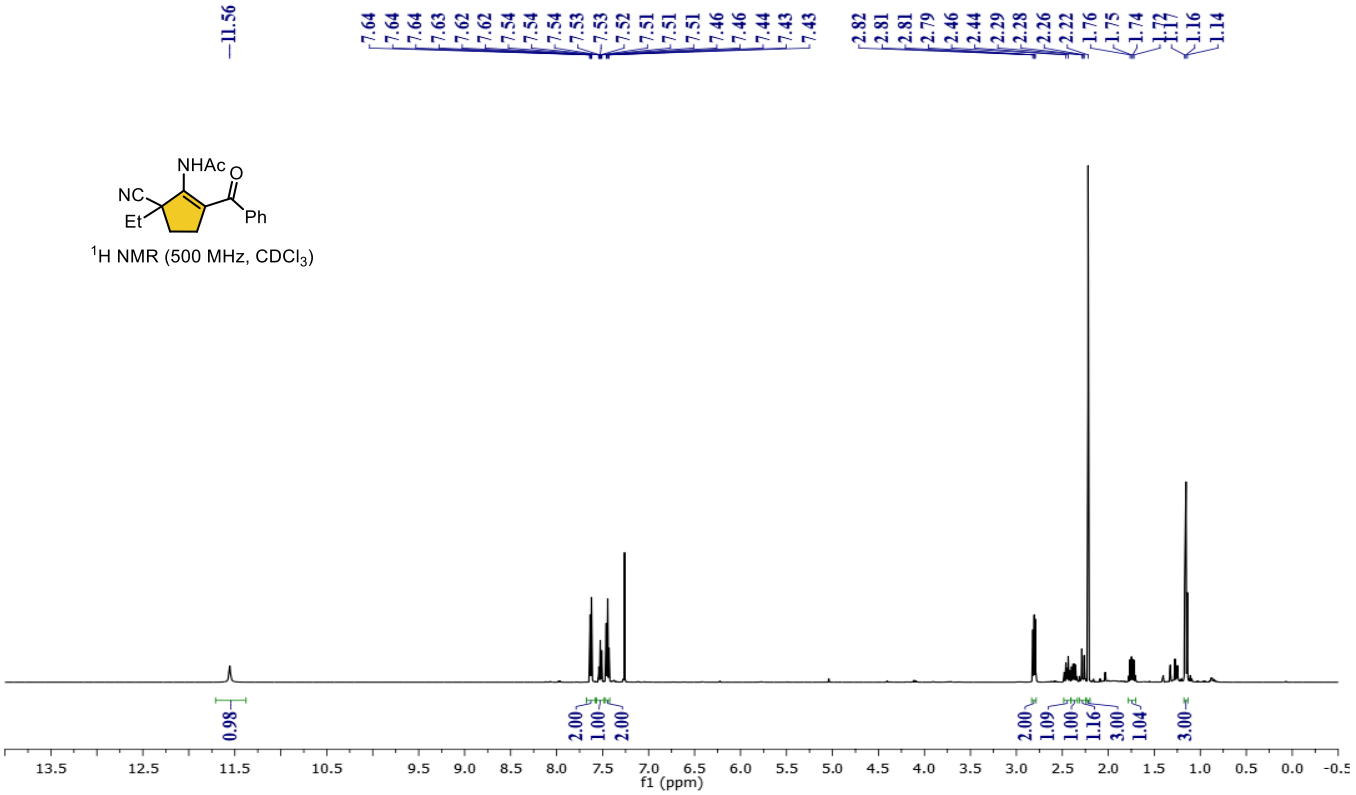


^{1}H NMR (400 MHz, $CDCl_3$)

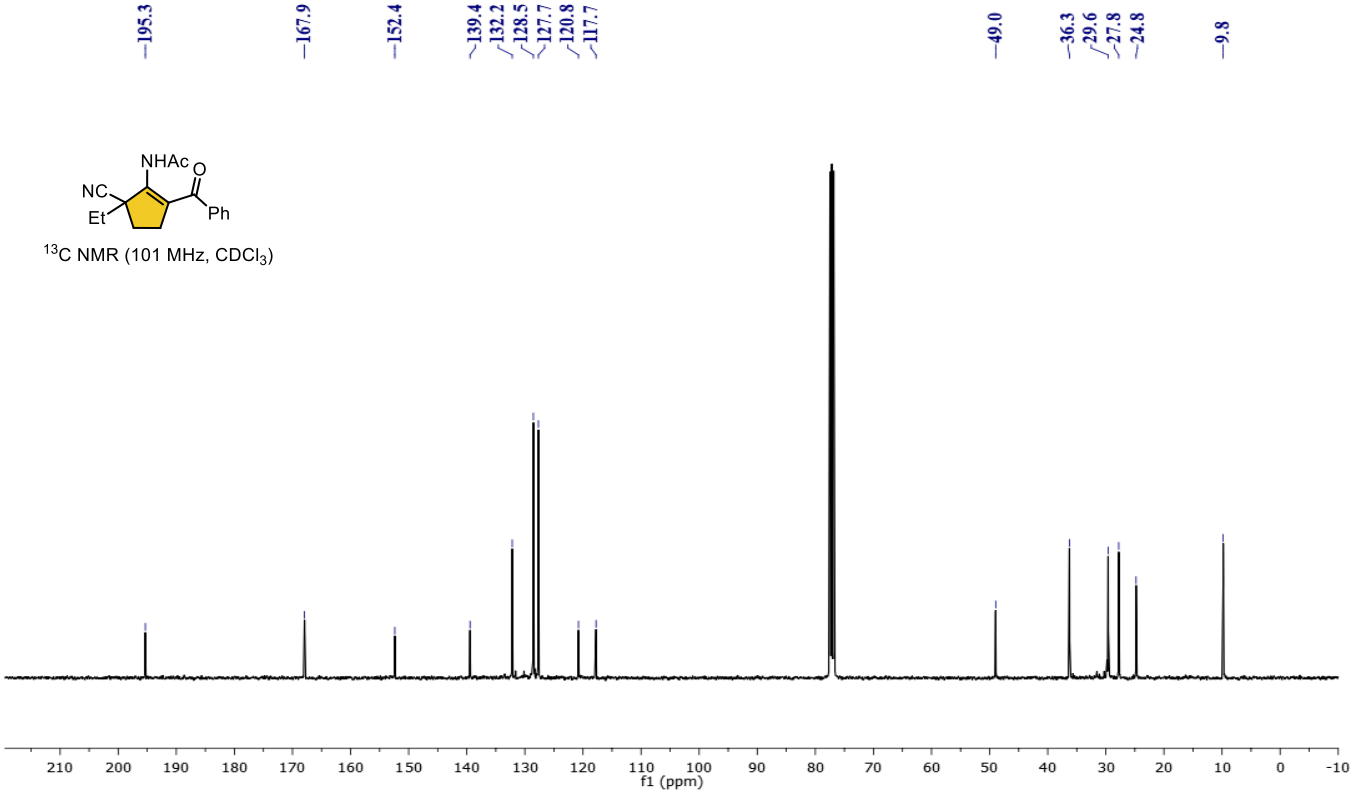


^{13}C NMR (101 MHz, $CDCl_3$)

N-(2-Benzoyl-5-cyano-5-ethylcyclopent-1-en-1-yl)acetamide (2o):

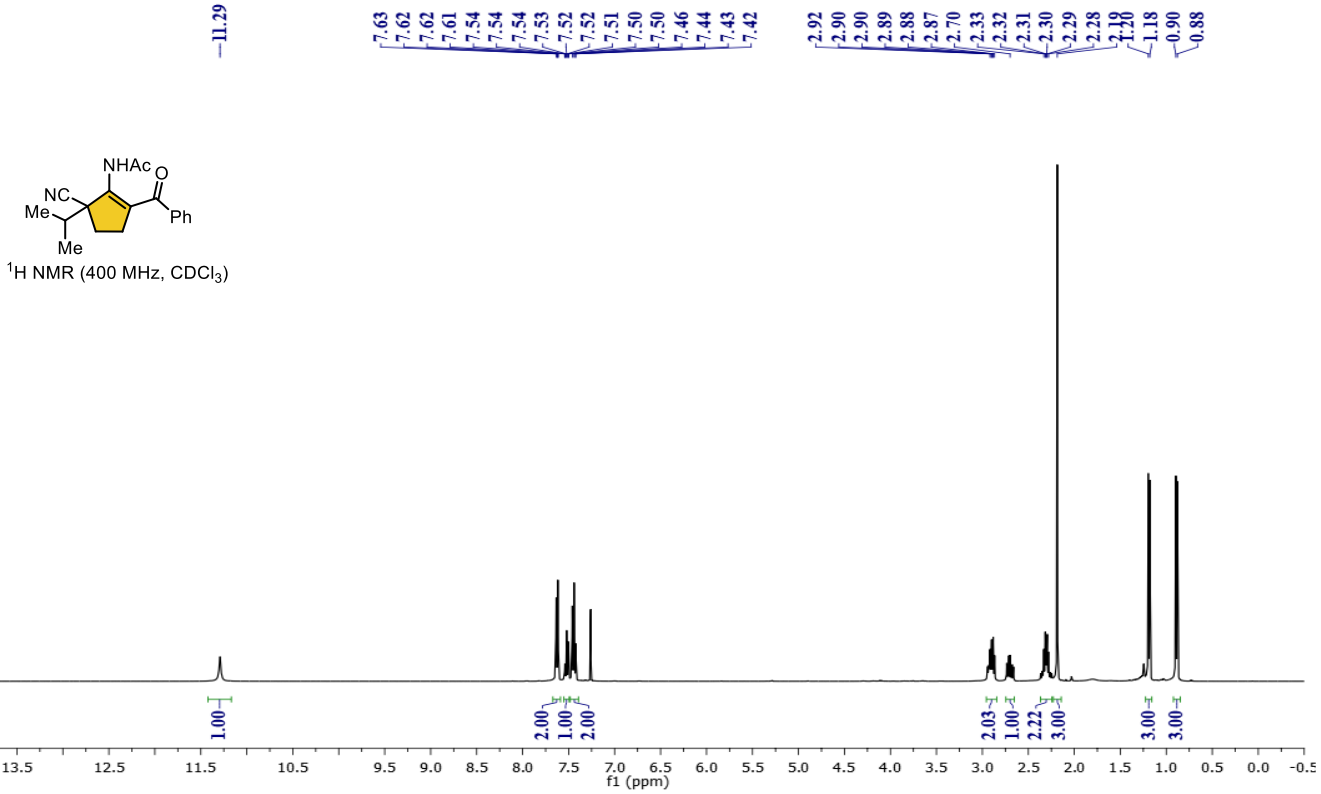


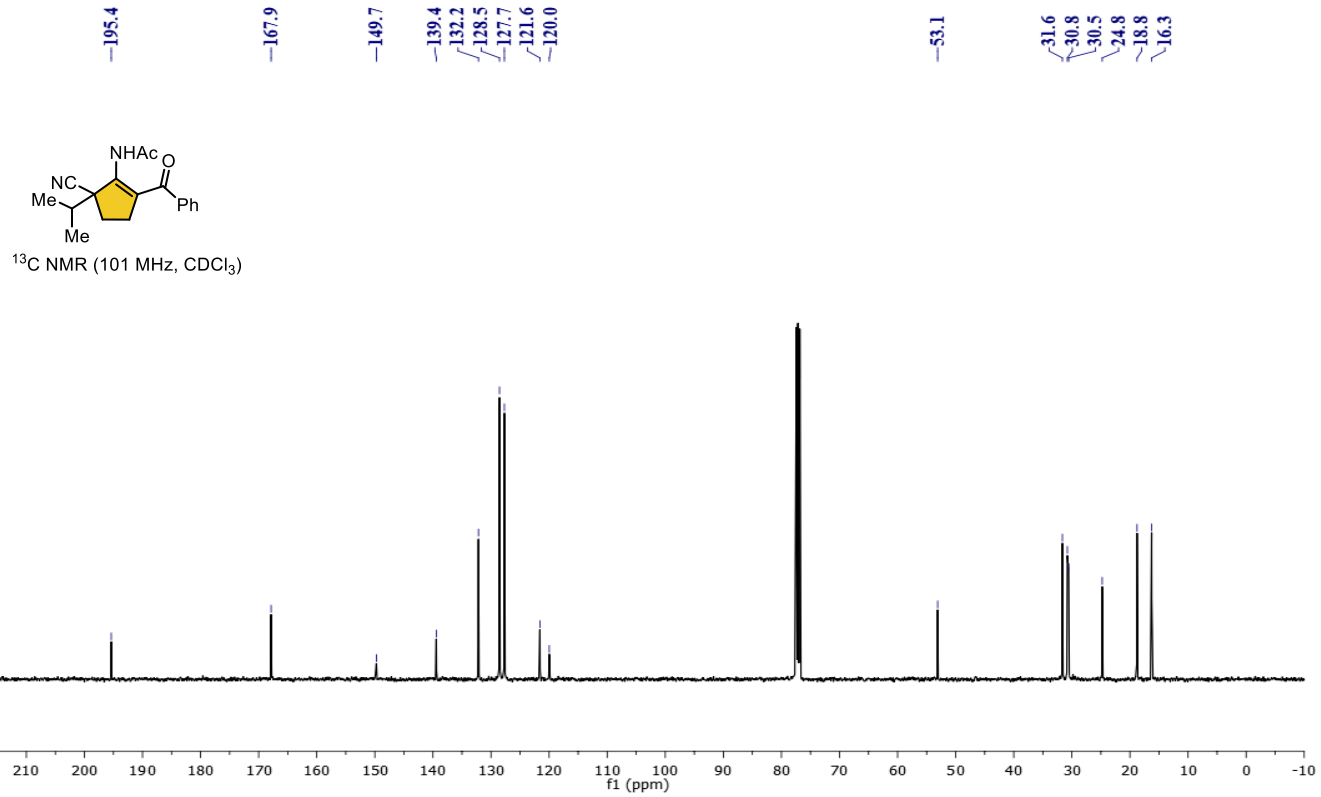
^{1}H NMR (500 MHz, $CDCl_3$)



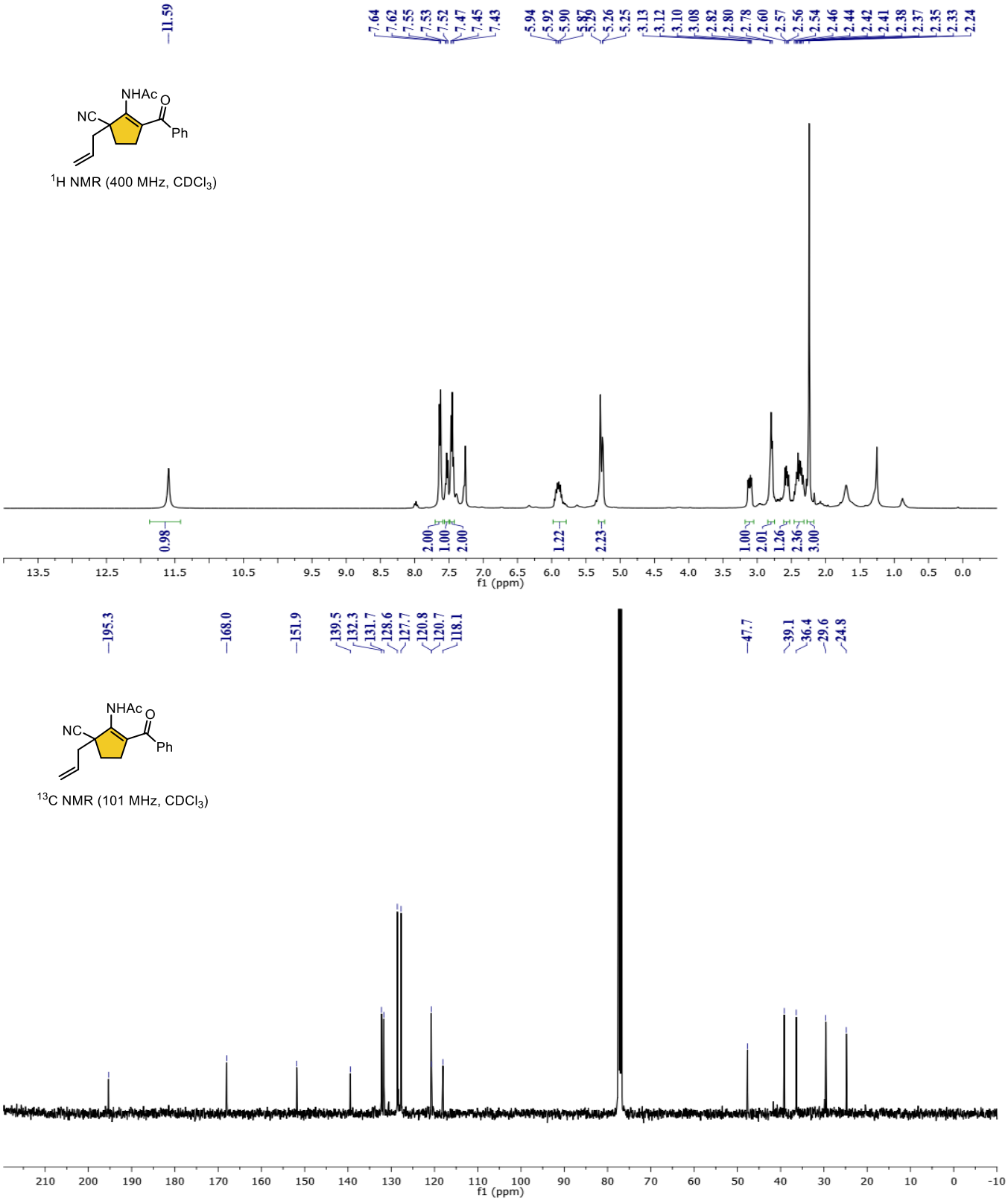
^{13}C NMR (101 MHz, $CDCl_3$)

N-(2-Benzoyl-5-cyano-5-isopropylcyclopent-1-en-1-yl)acetamide (2p):

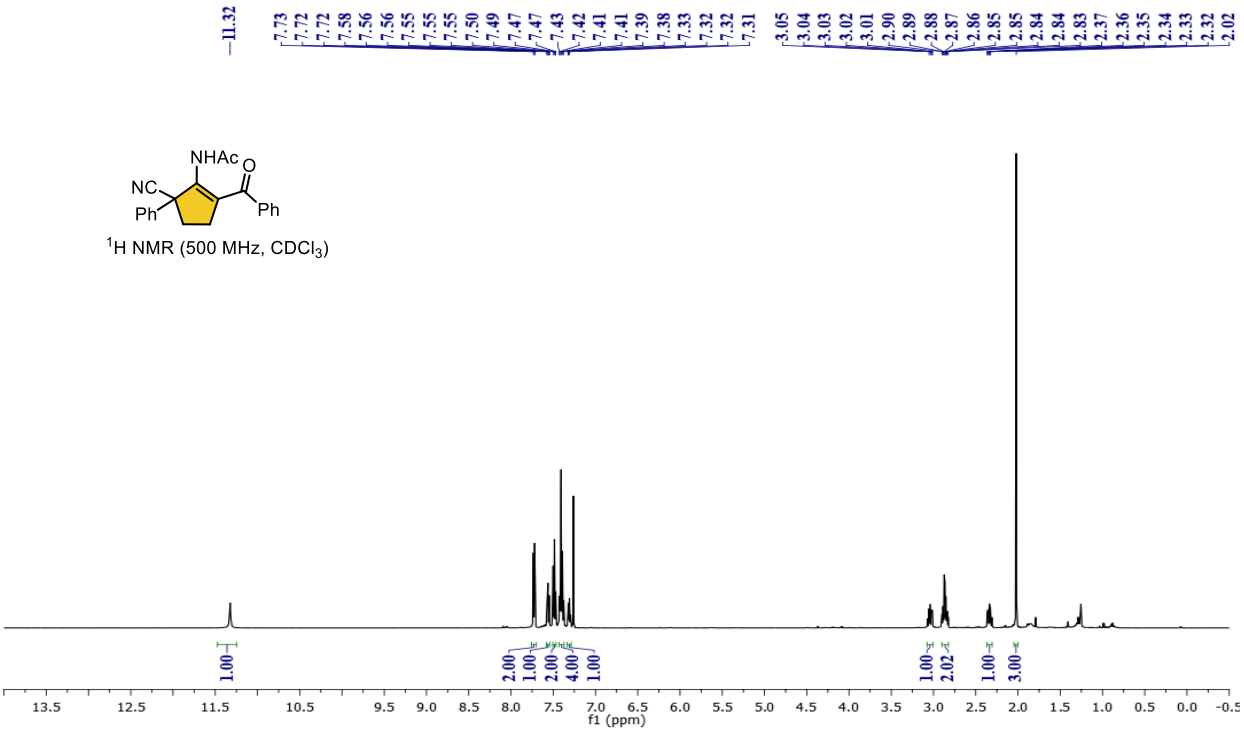


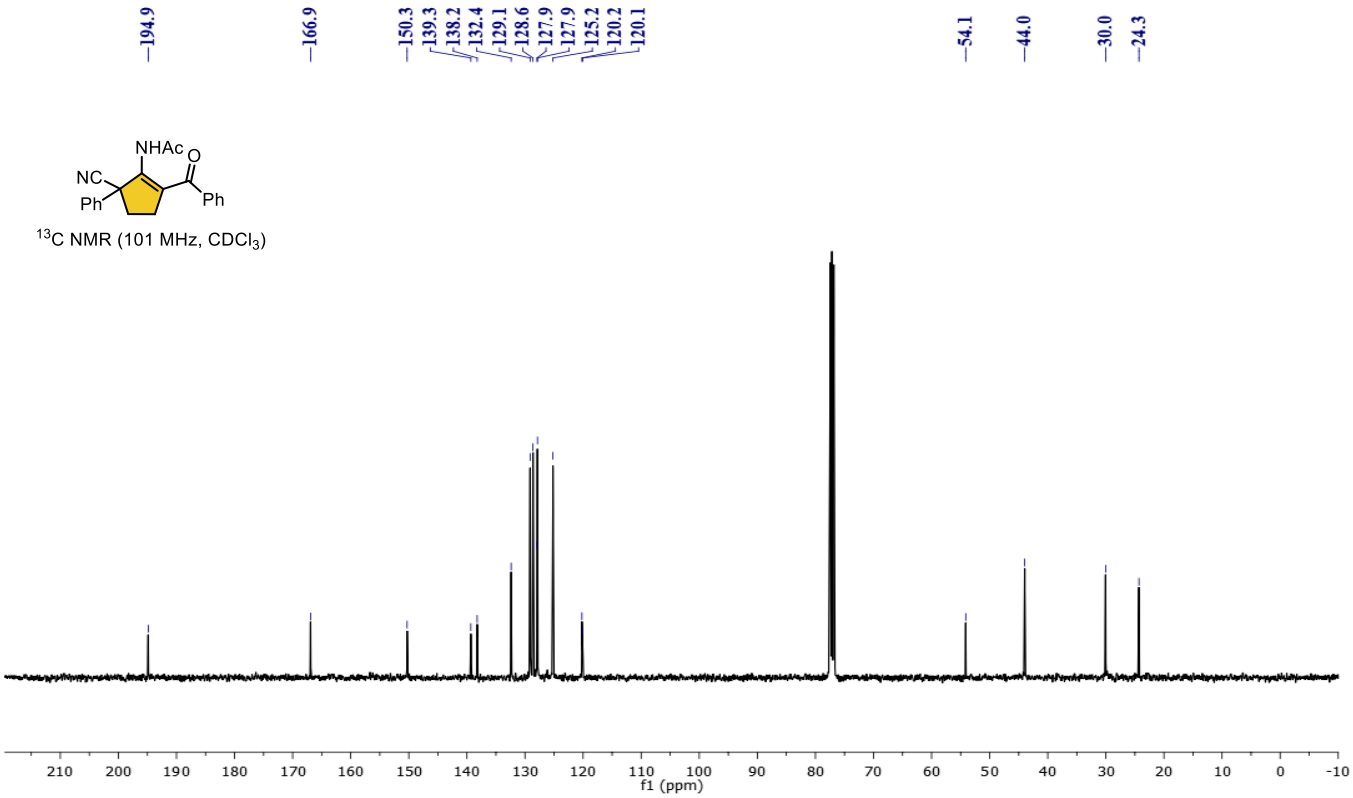


N-(5-Allyl-2-benzoyl-5-cyanocyclopent-1-en-1-yl)acetamide (2q):

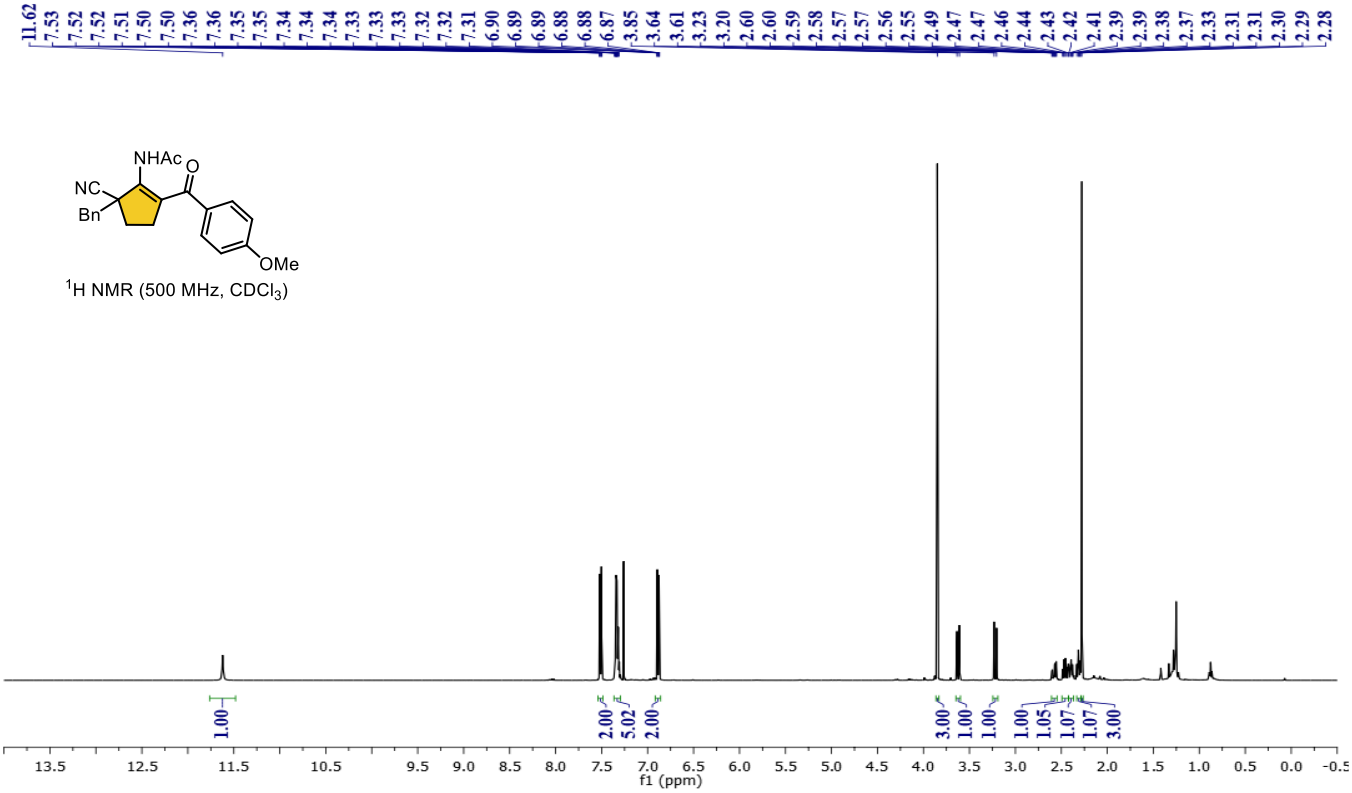


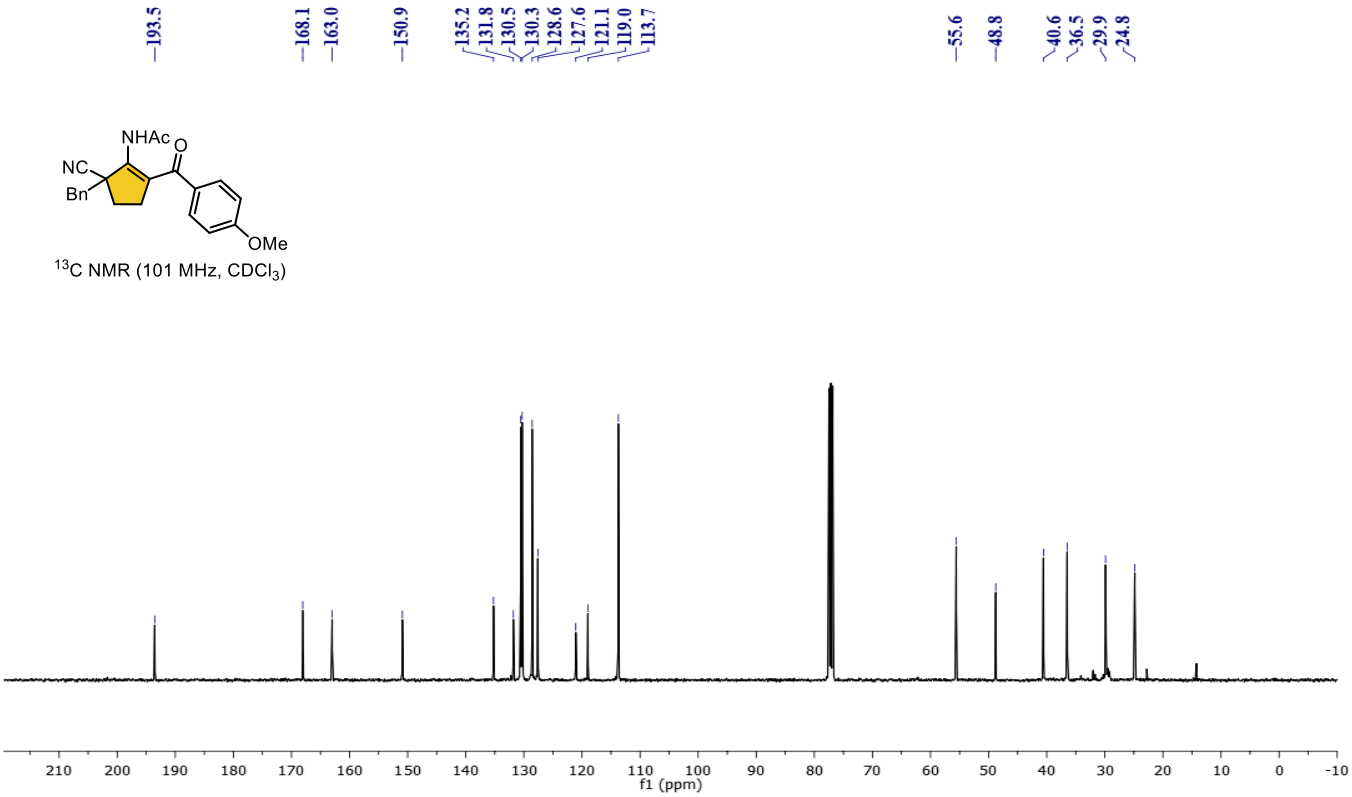
***N*-(2-benzoyl-5-cyano-5-phenylcyclopent-1-en-1-yl)acetamide (2r):**



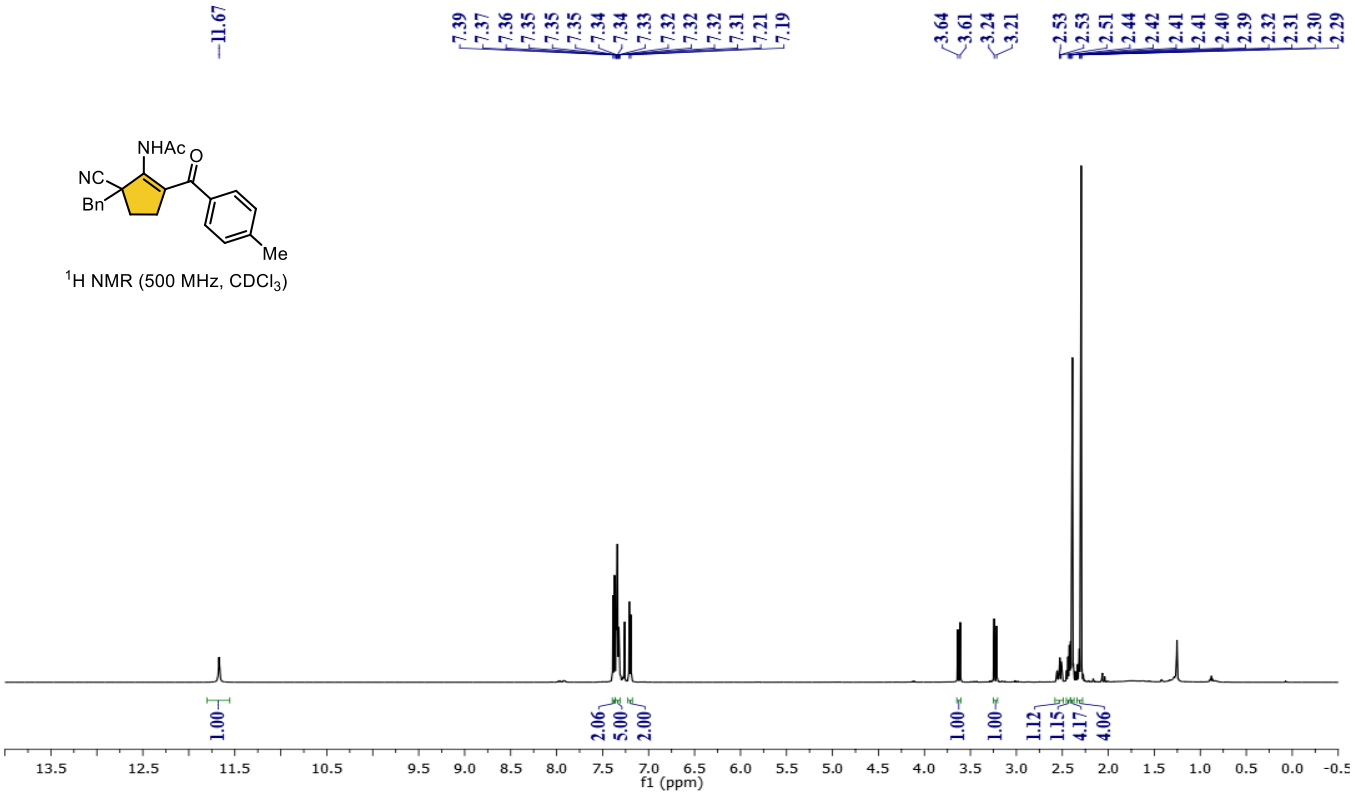


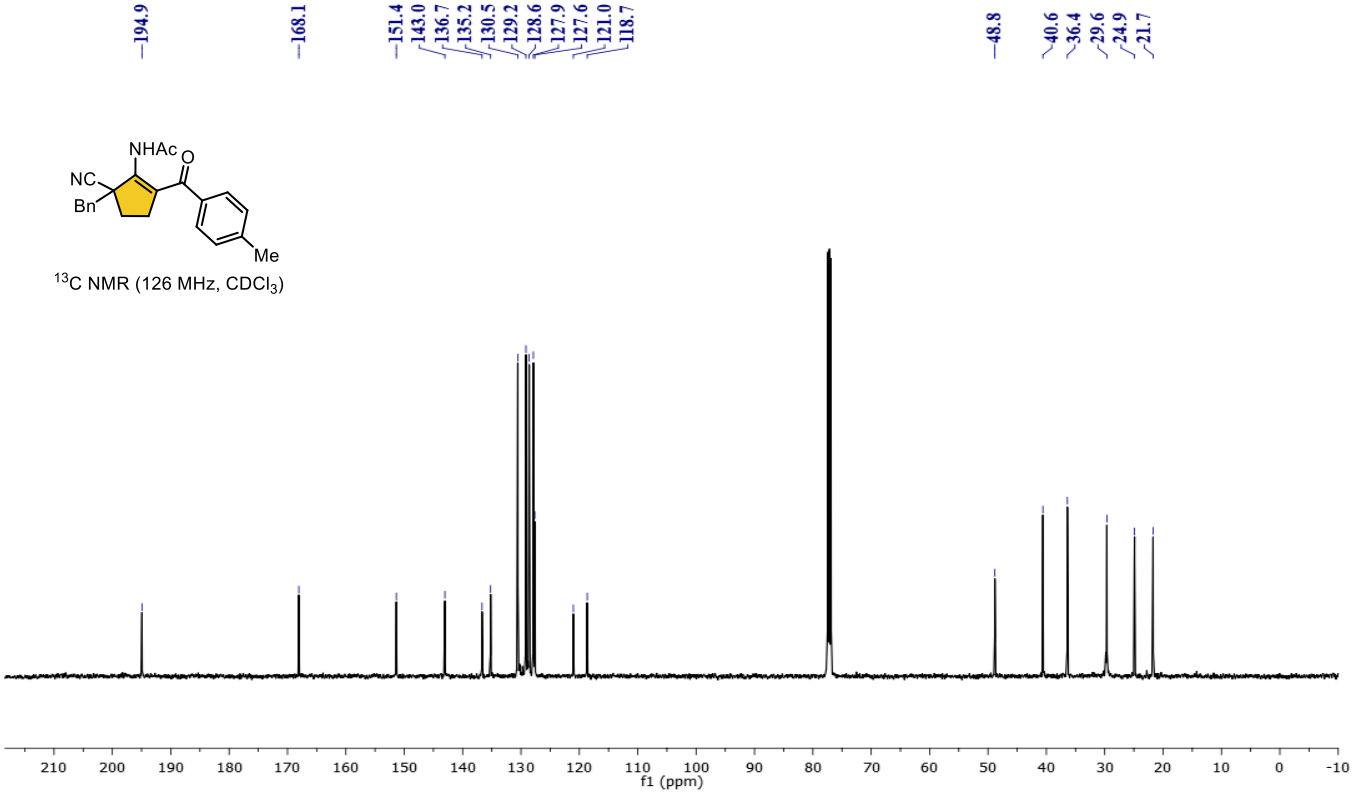
***N*-(5-Benzyl-5-cyano-2-(4-methoxybenzoyl)cyclopent-1-en-1-yl)acetamide (2s):**



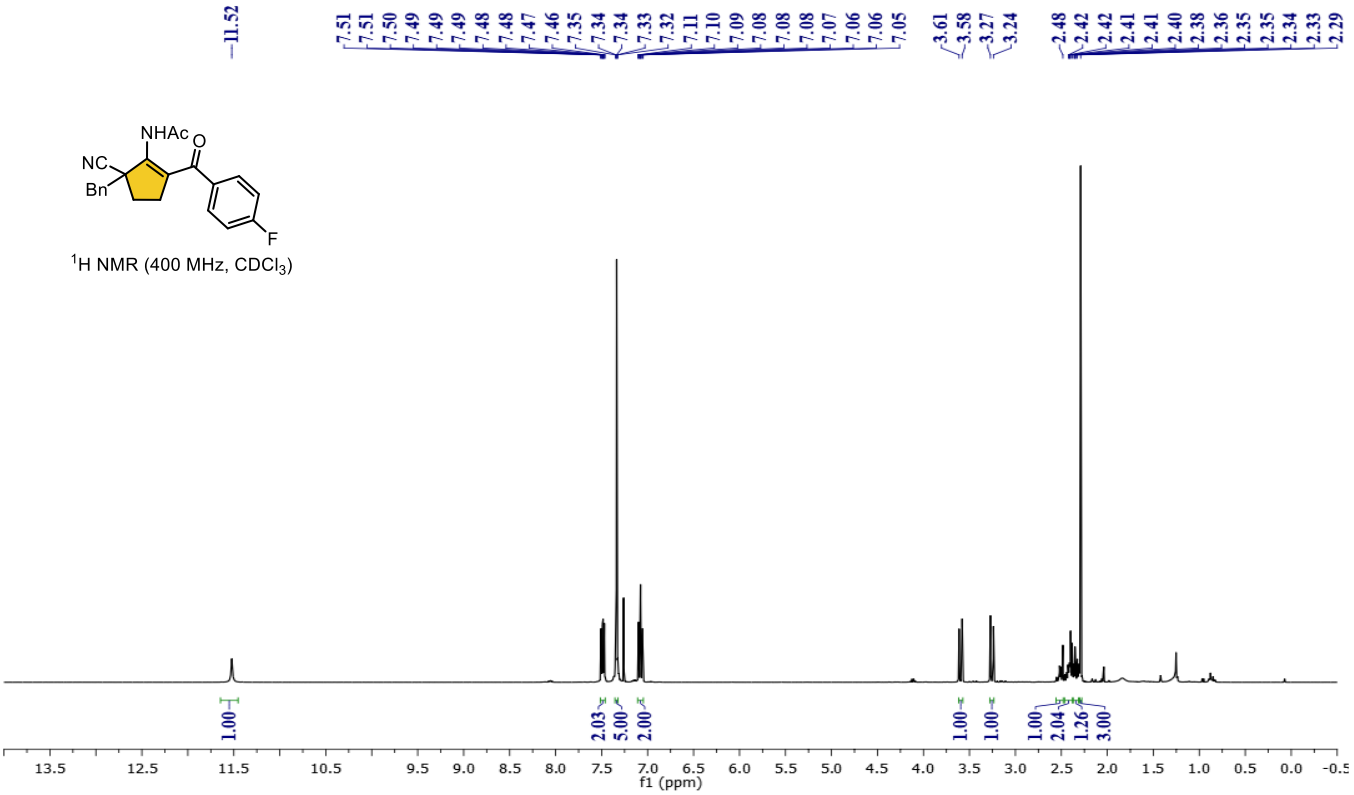


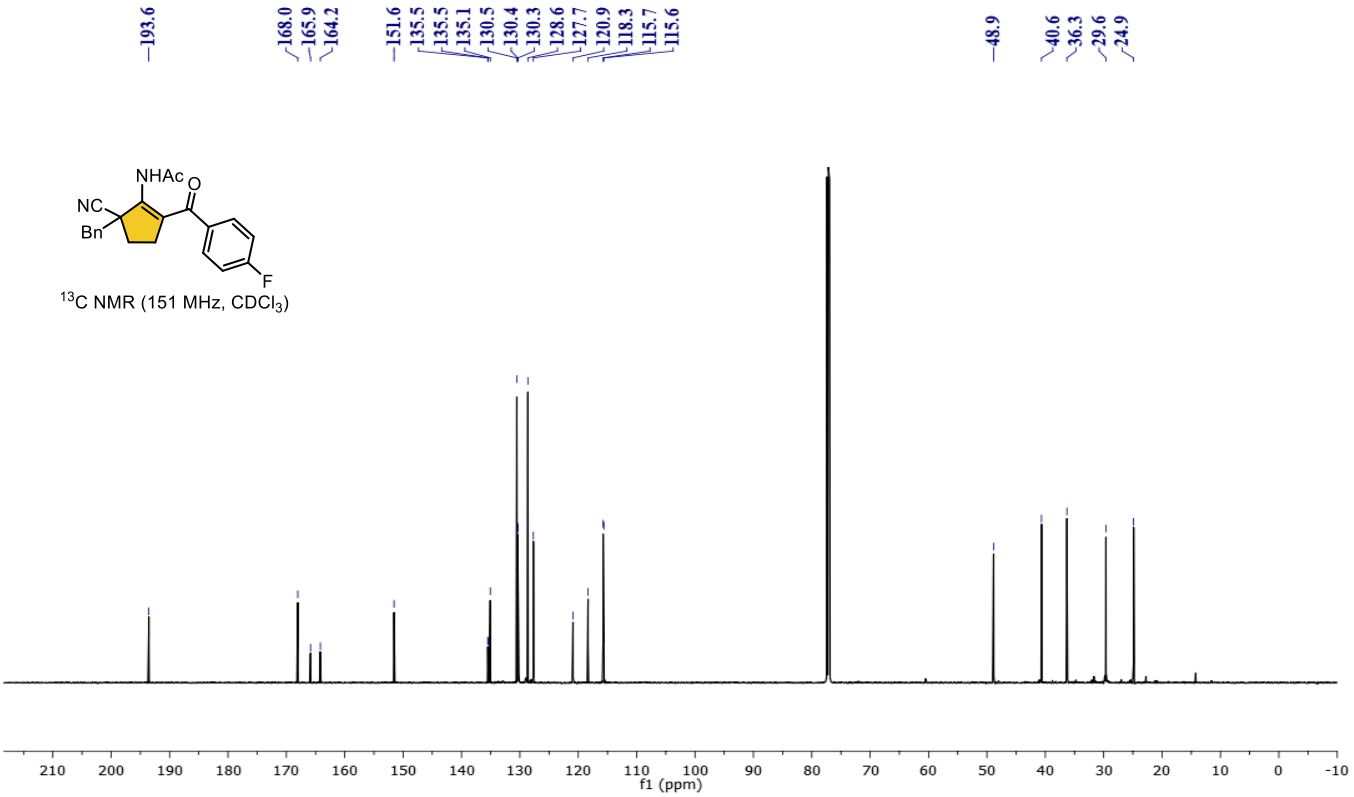
***N*-(5-Benzyl-5-cyano-2-(4-methylbenzoyl)cyclopent-1-en-1-yl)acetamide (2t):**

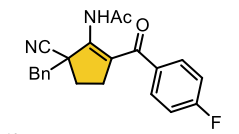




_N_-(5-Benzyl-5-cyano-2-(4-fluorobenzoyl)cyclopent-1-en-1-yl)acetamide (2u):

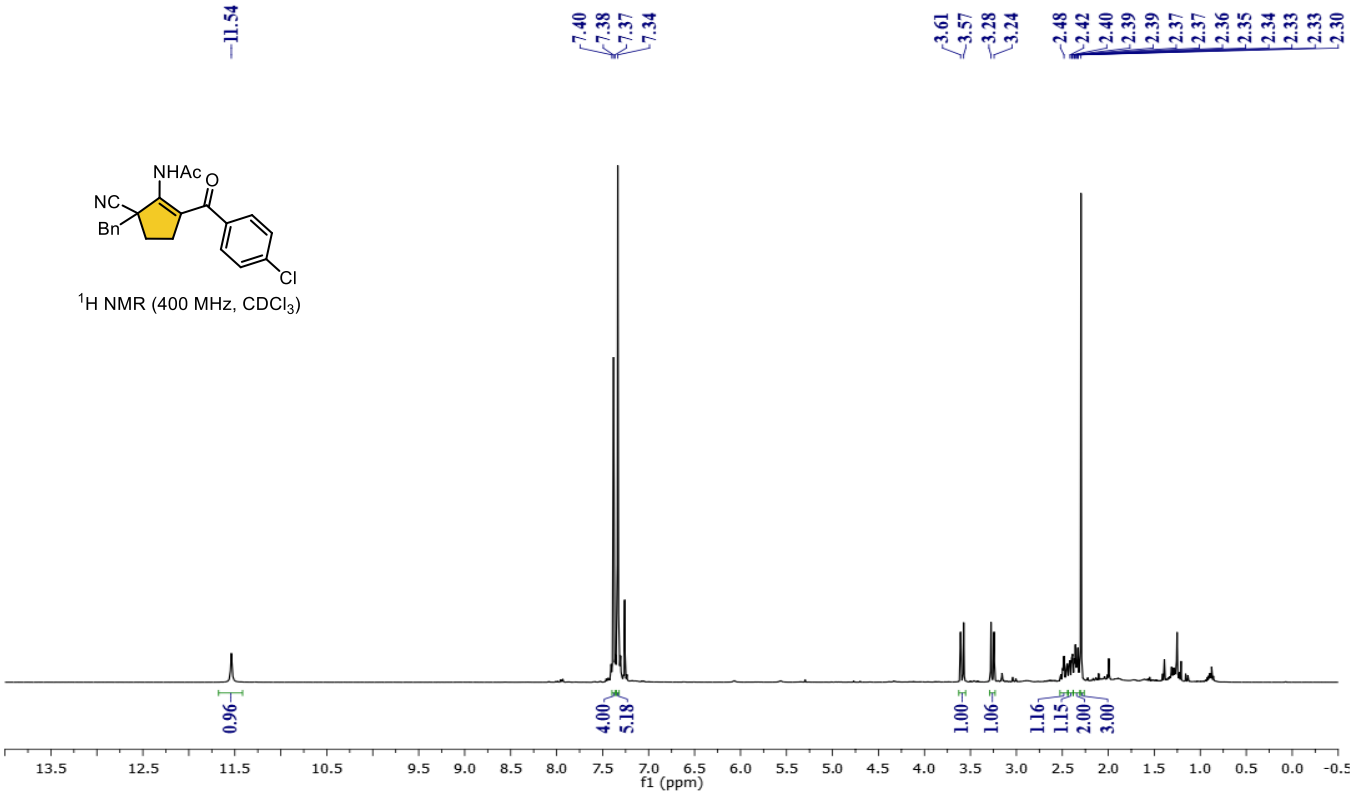




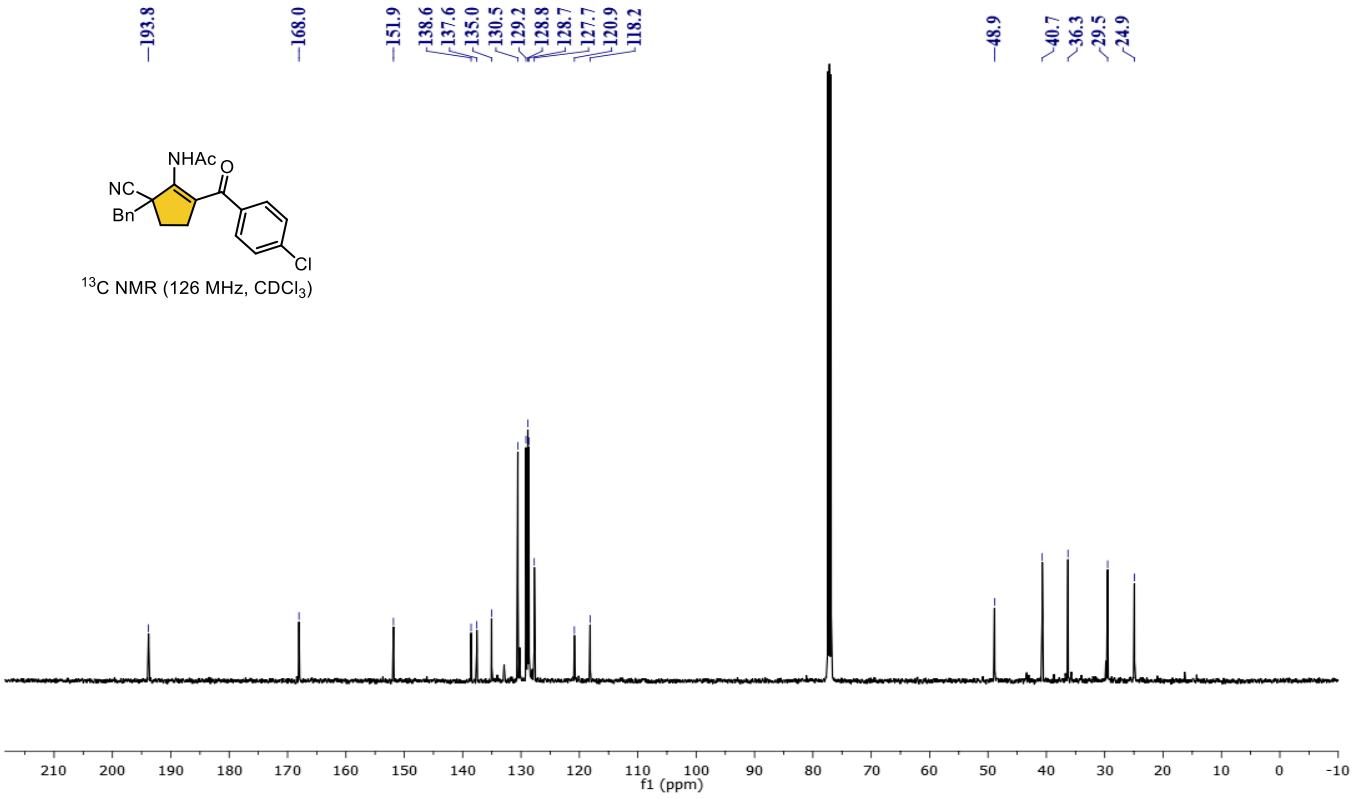


^{19}F NMR (377 MHz, $CDCl_3$)

***N*-(5-Benzyl-2-(4-chlorobenzoyl)-5-cyanocyclopent-1-en-1-yl)acetamide (2v):**

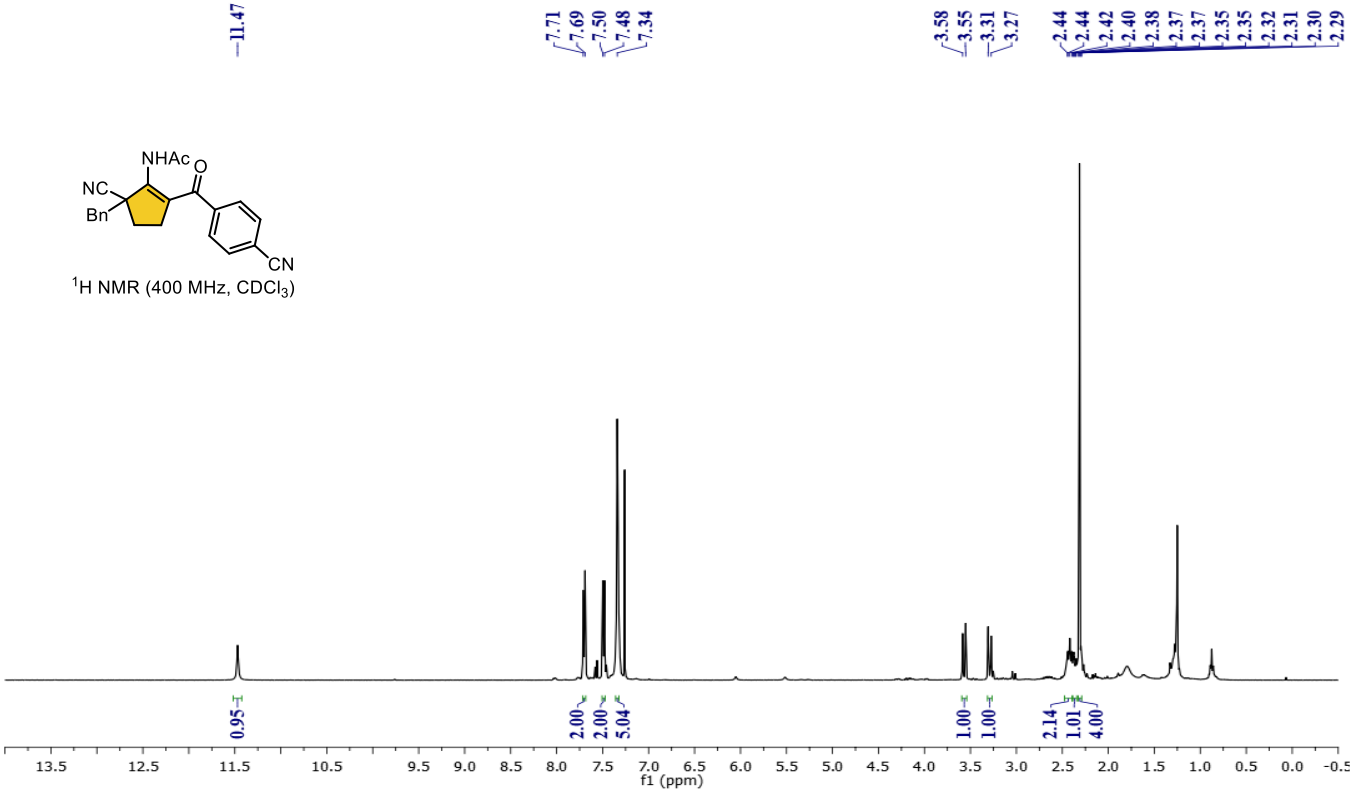


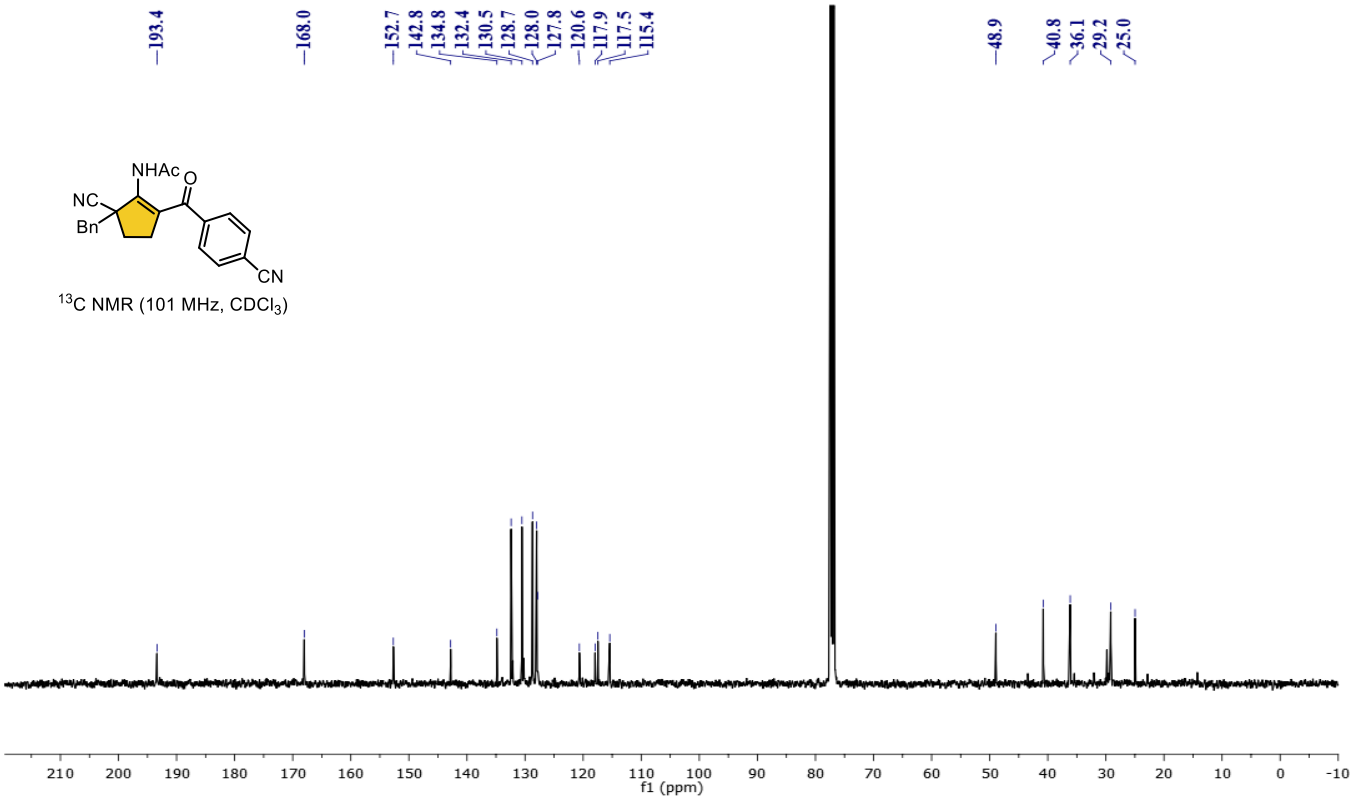
^{1}H NMR (400 MHz, $CDCl_3$)



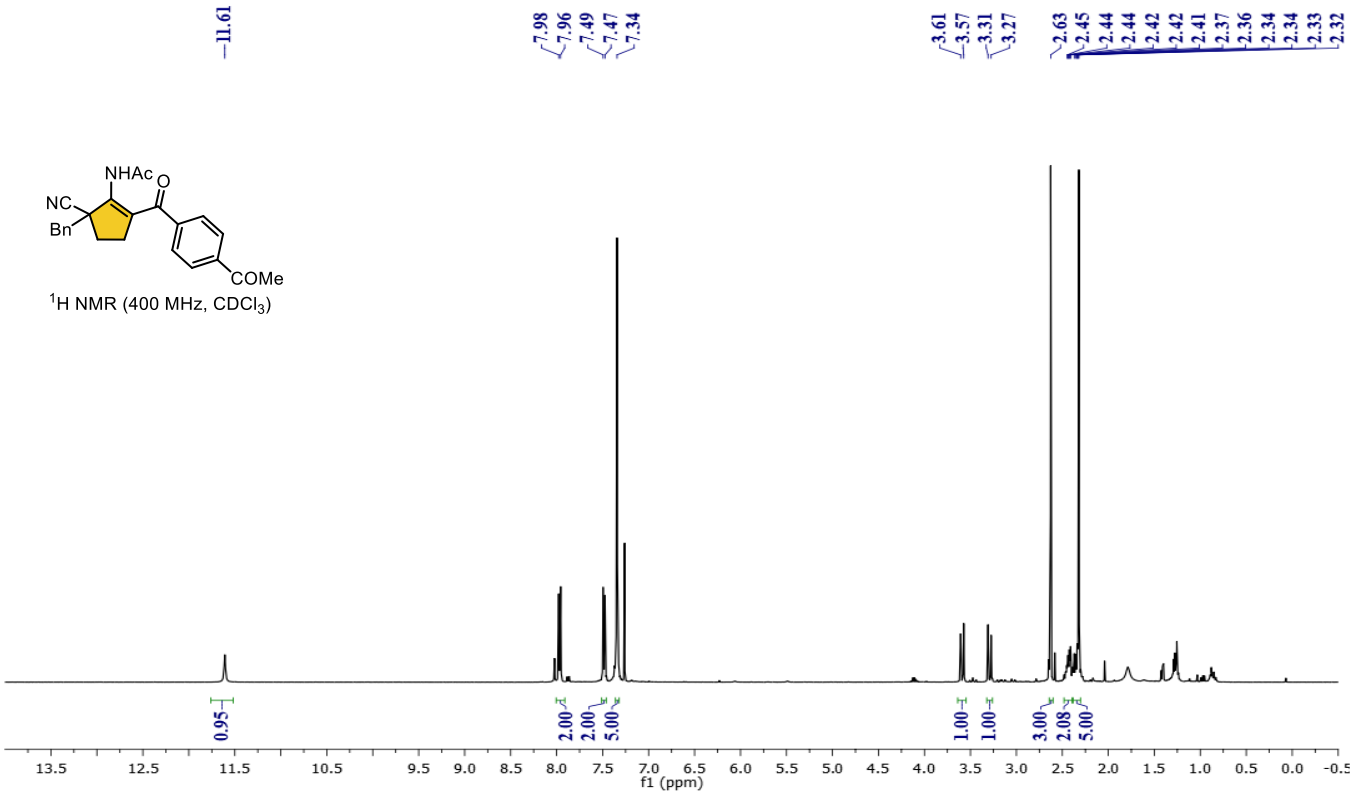
^{13}C NMR (126 MHz, $CDCl_3$)

***N*-(2-Benzoyl-5-benzyl-5-cyanocyclopent-1-en-1-yl)-2-chloroacetamide (2w):**

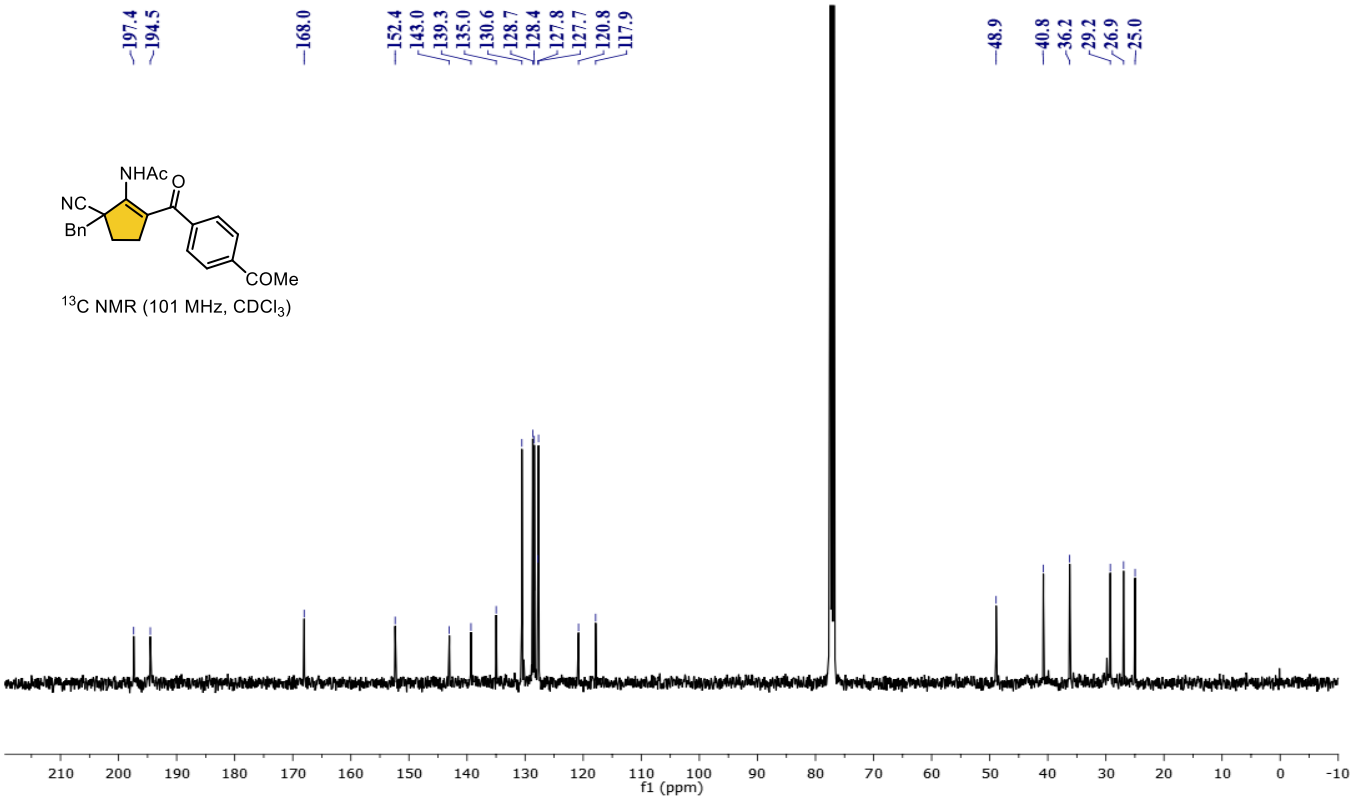




***N*-(2-(4-Acetylbenzoyl)-5-benzyl-5-cyanocyclopent-1-en-1-yl)acetamide (2x):**

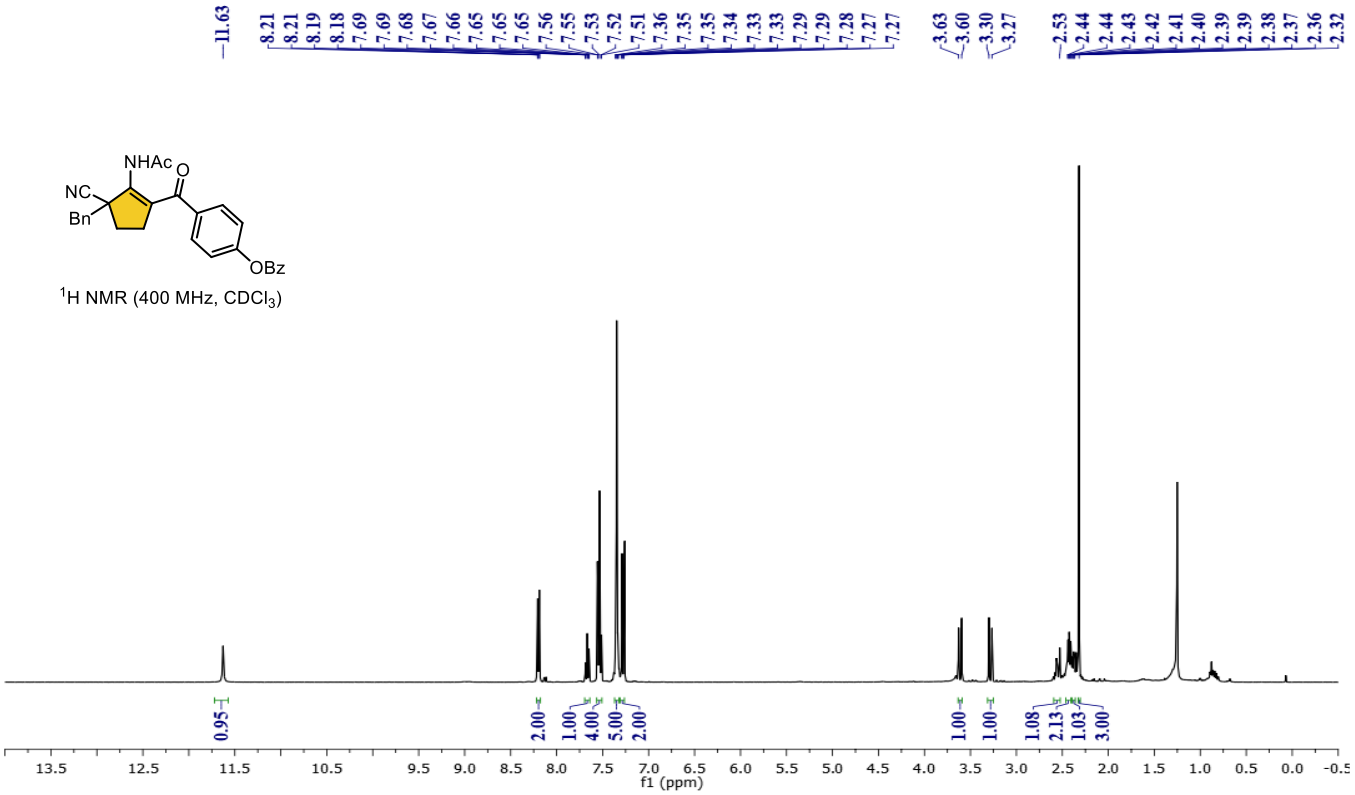


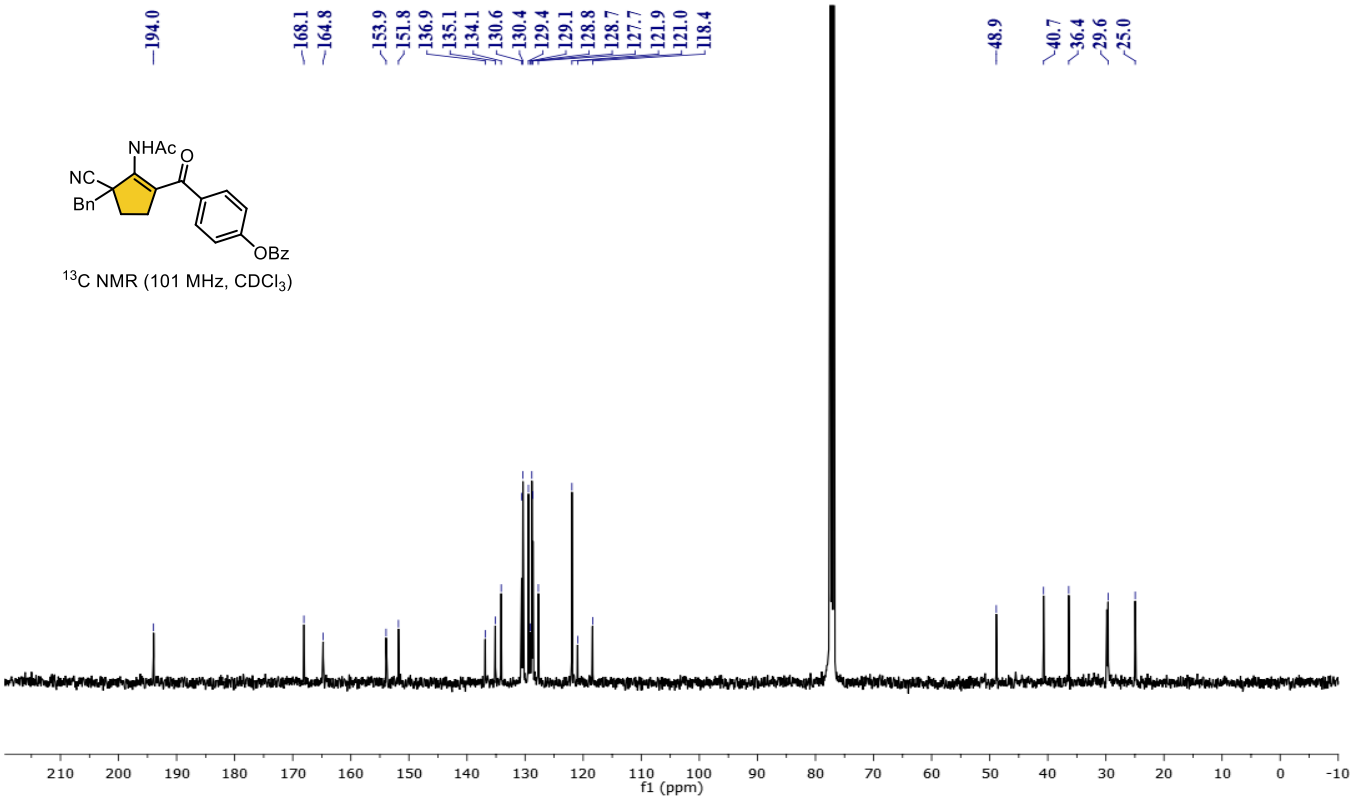
^{1}H NMR (400 MHz, $CDCl_3$)



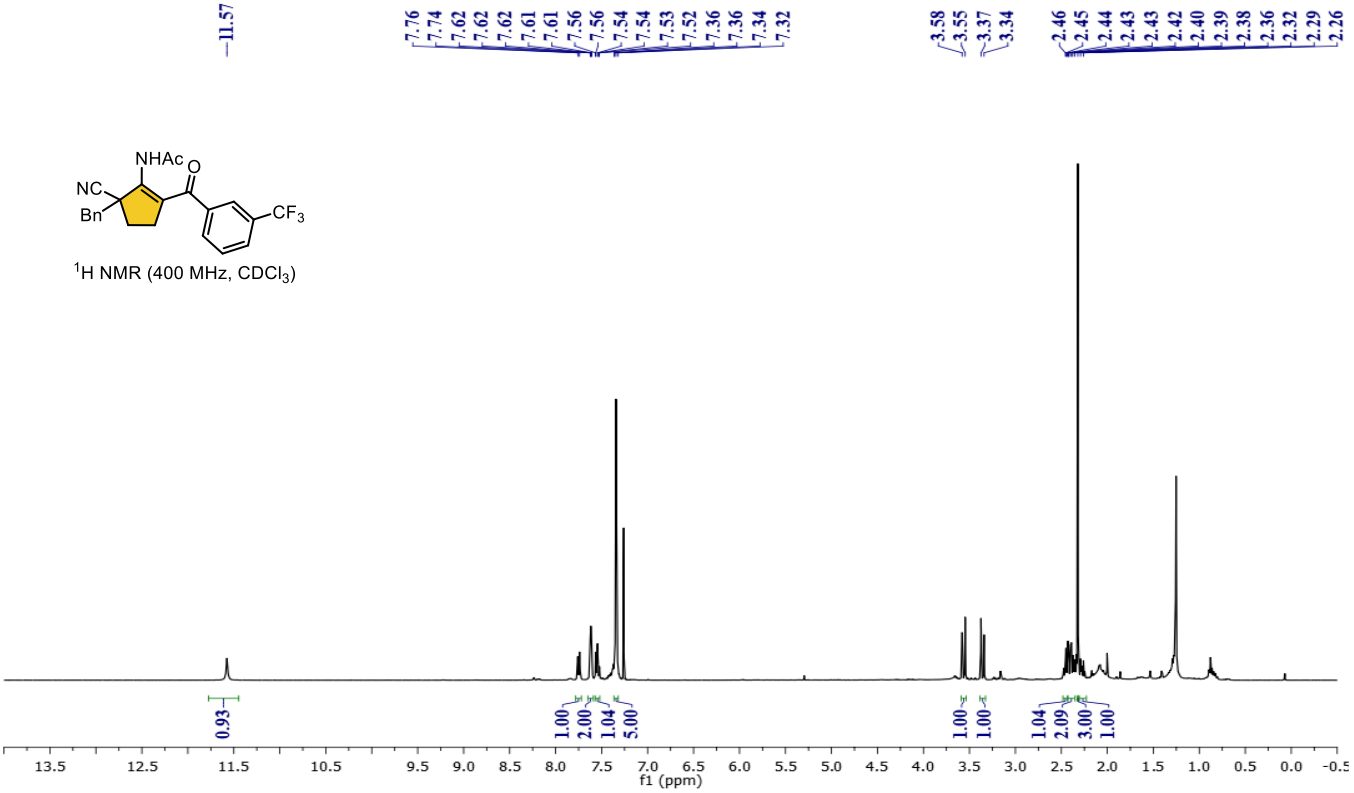
^{13}C NMR (101 MHz, $CDCl_3$)

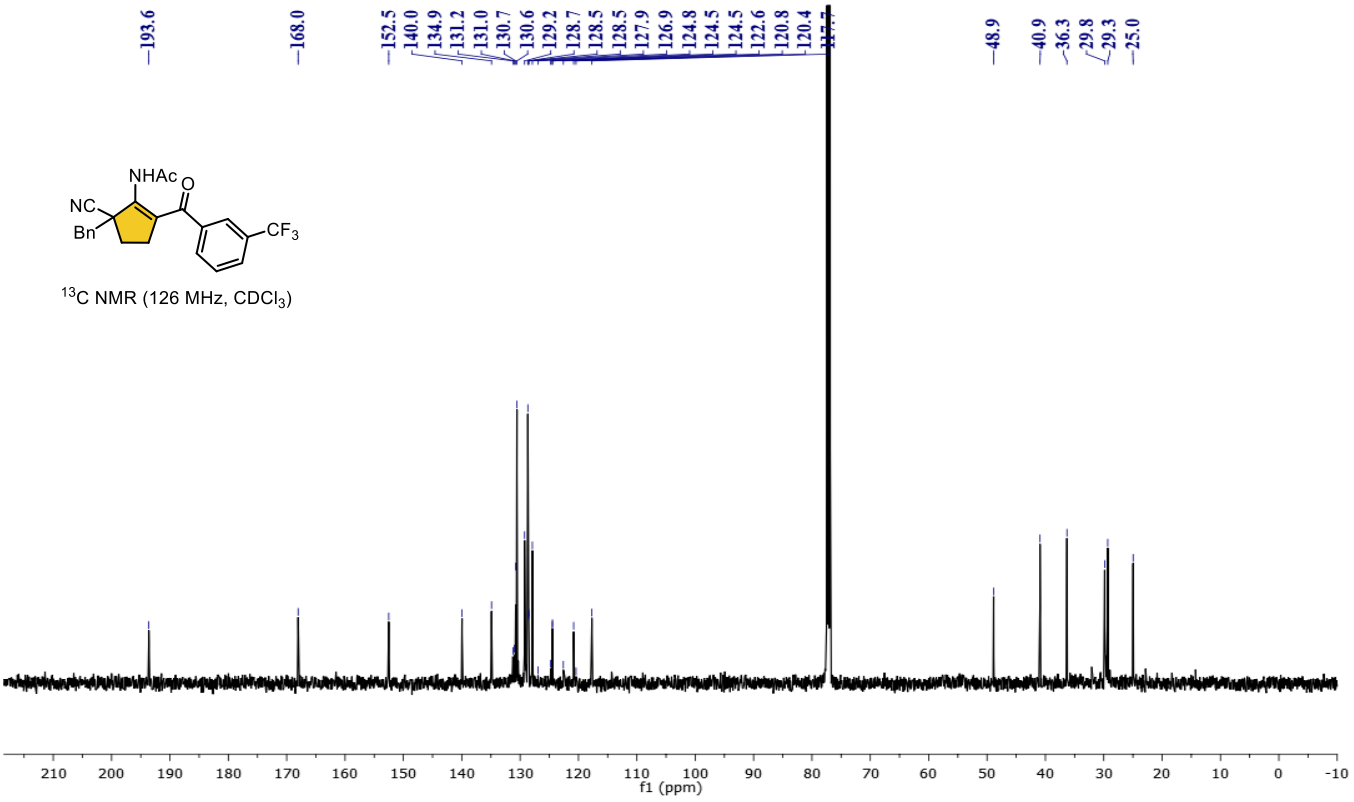
4-(2-acetamido-3-benzyl-3-cyanocyclopent-1-ene-1-carbonyl)phenyl benzoate (2y):

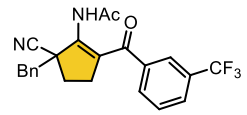




***N*-(5-Benzyl-5-cyano-2-(3-(trifluoromethyl)benzoyl)cyclopent-1-en-1-yl)acetamide (2z):**

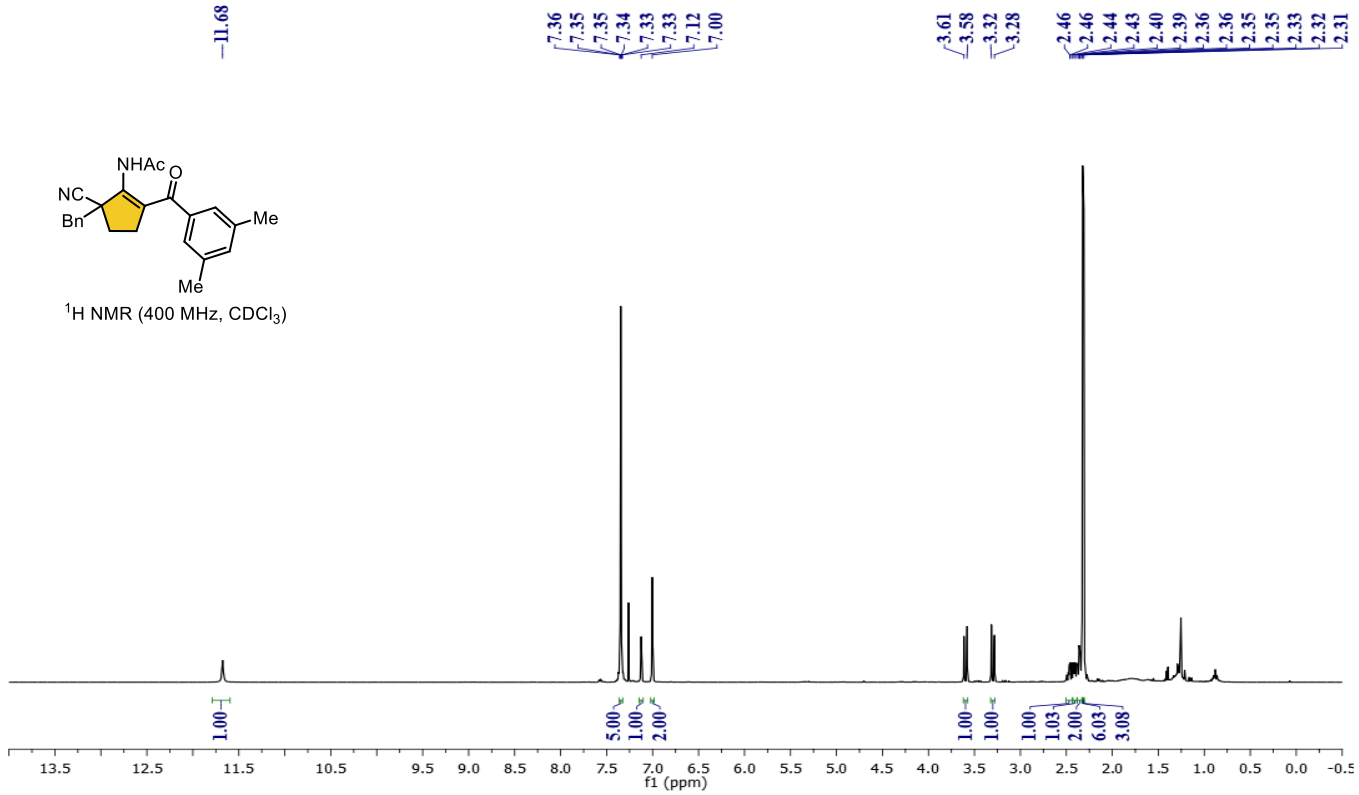


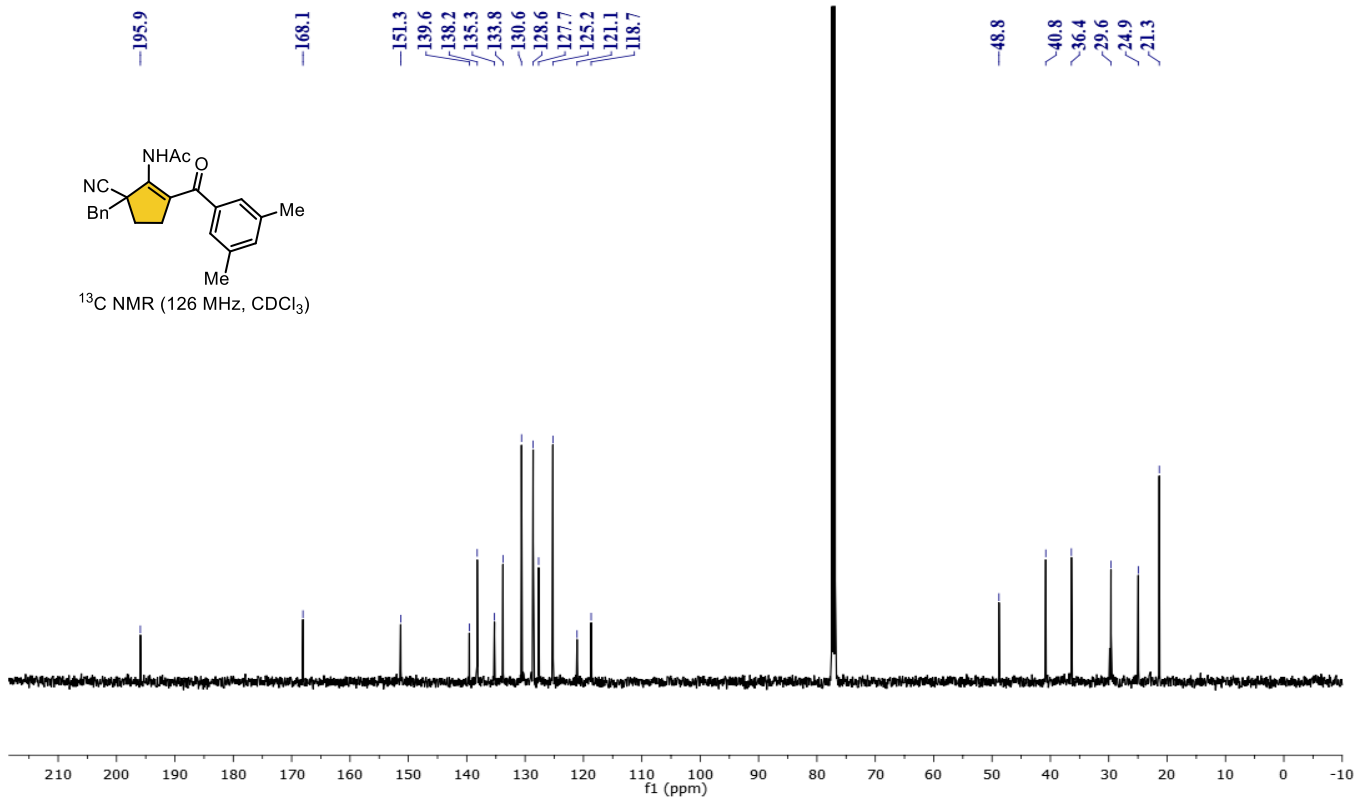




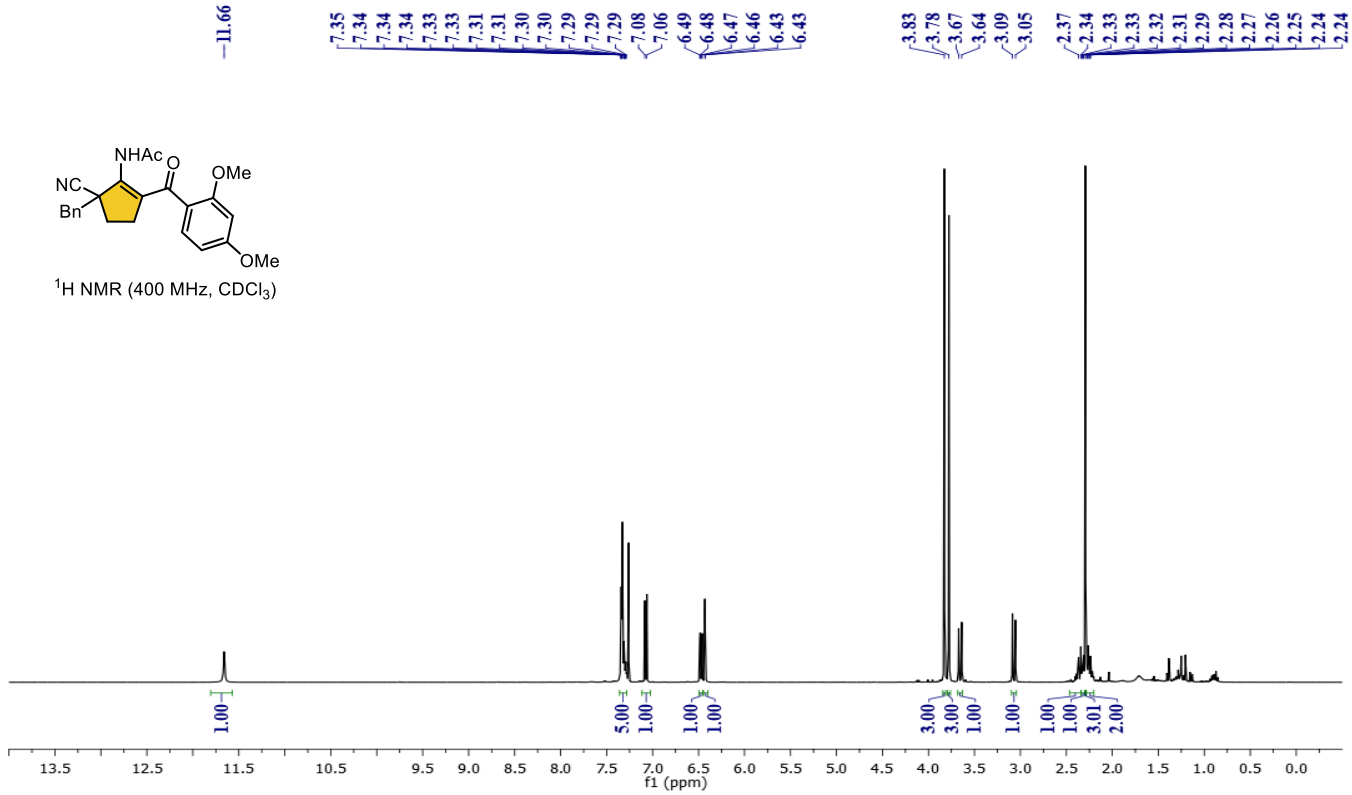
^{19}F NMR (376 MHz, $CDCl_3$)

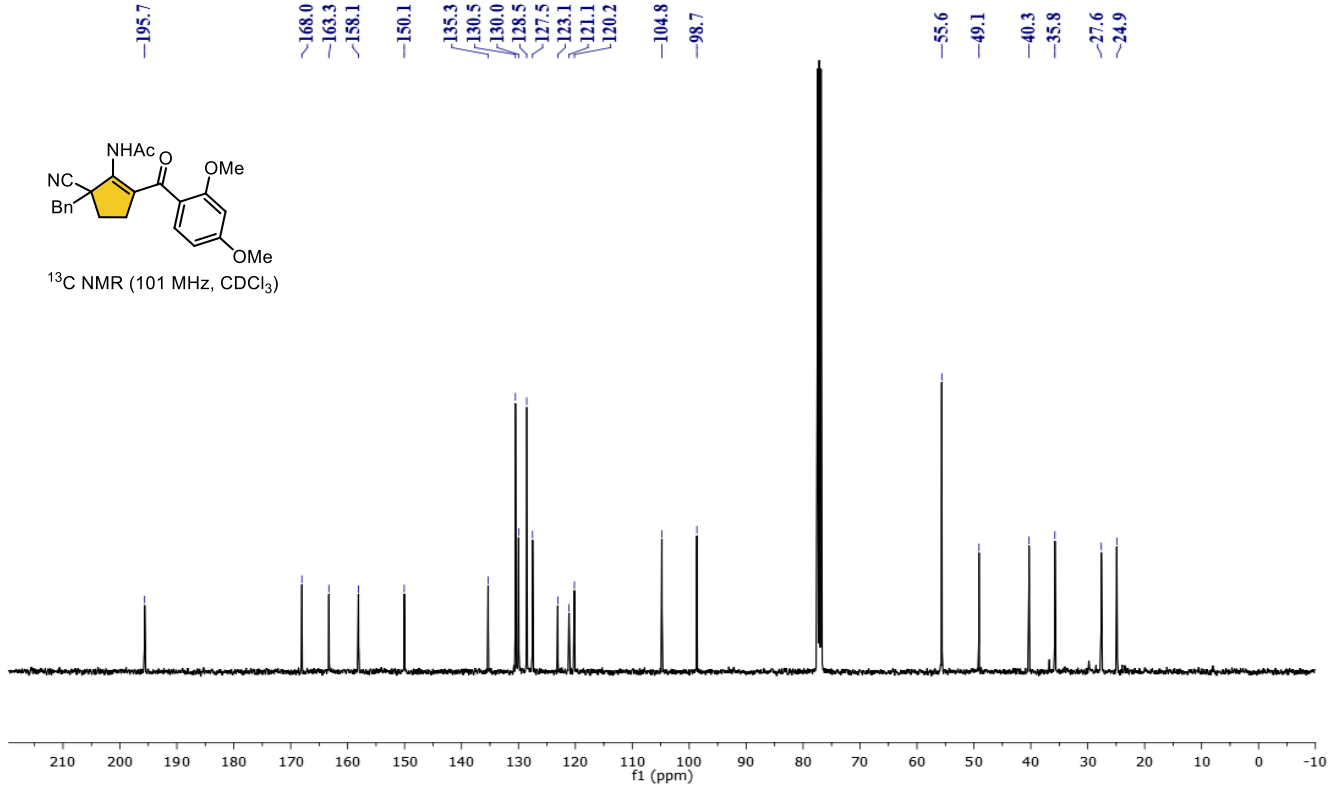
***N*-(5-Benzyl-5-cyano-2-(3,5-dimethylbenzoyl)cyclopent-1-en-1-yl)acetamide (2aa):**



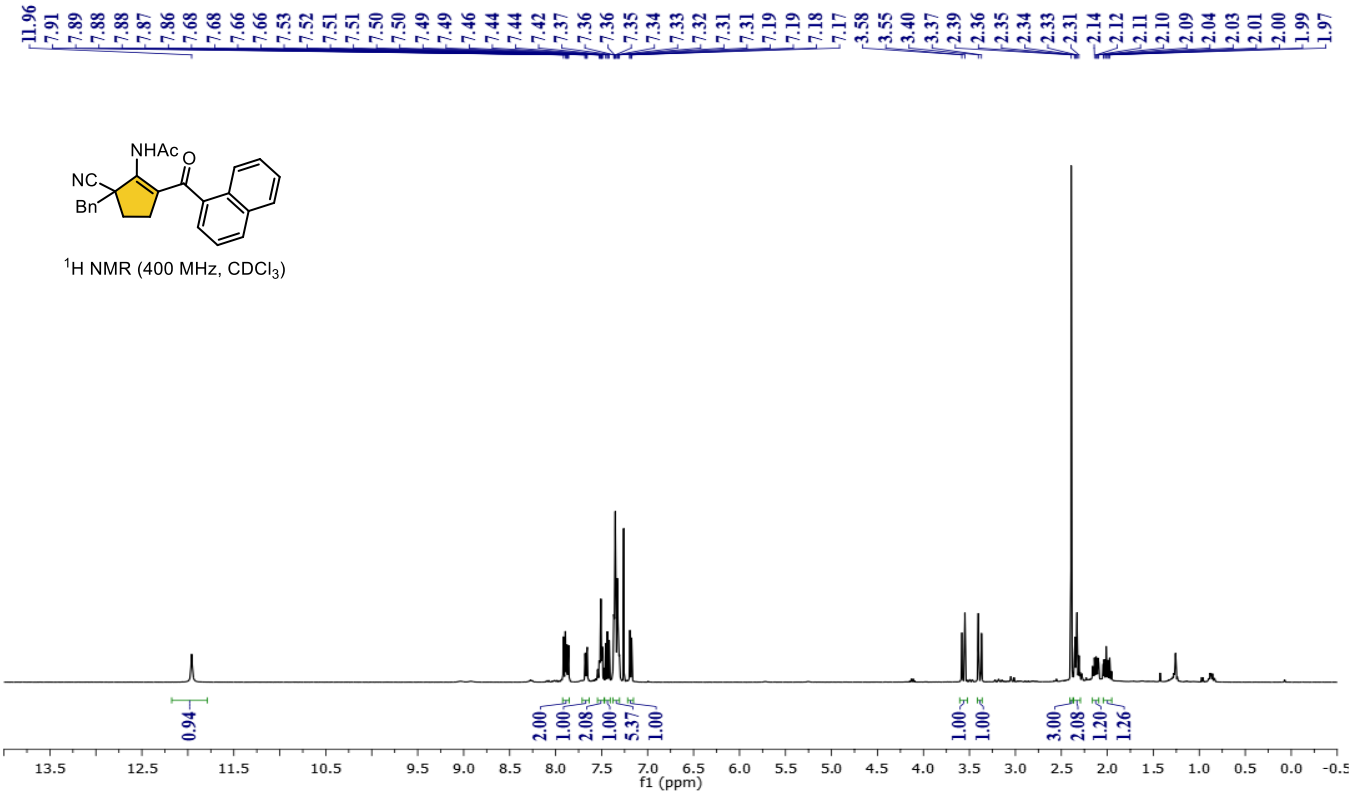


_N_-(5-Benzyl-5-cyano-2-(2,4-dimethoxybenzoyl)cyclopent-1-en-1-yl)acetamide (2ab):

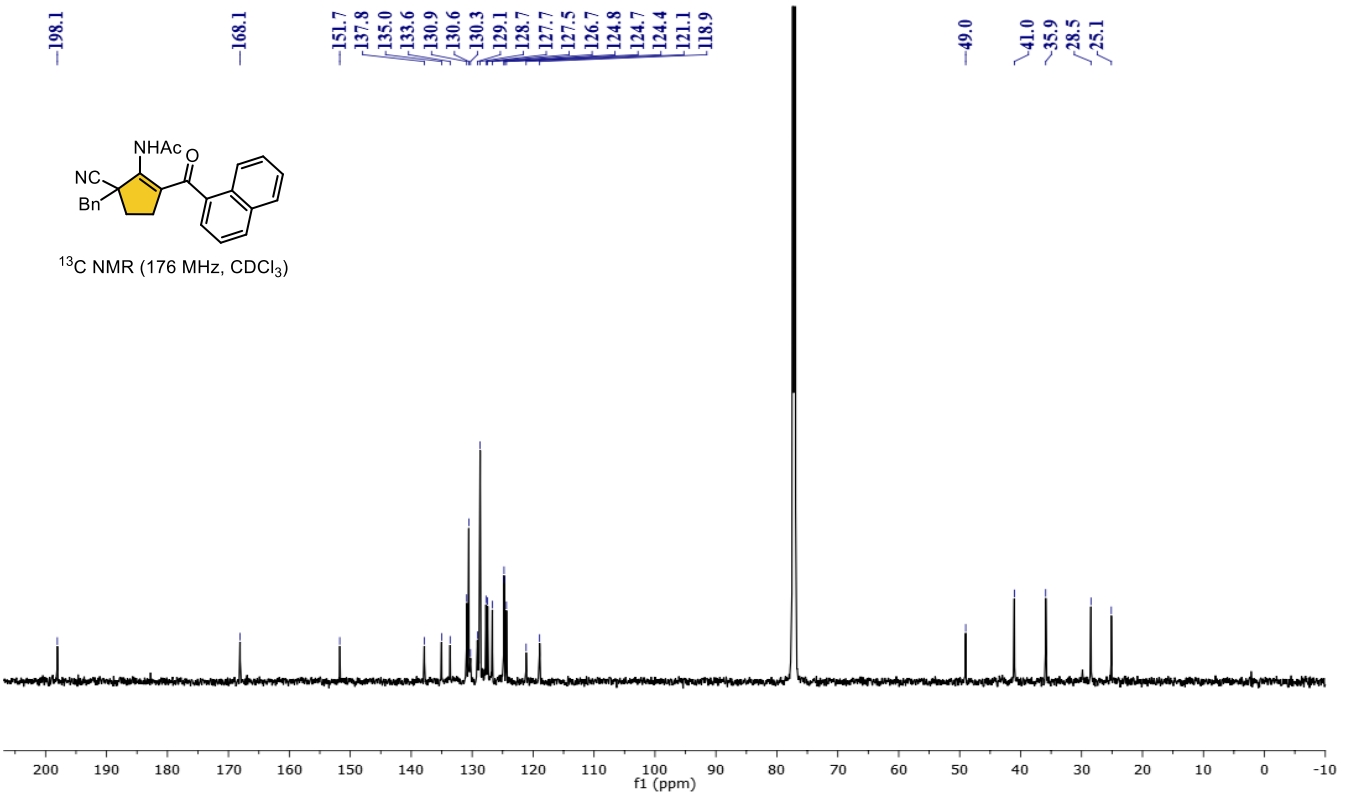




***N*-(2-(1-Naphthoyl)-5-benzyl-5-cyanocyclopent-1-en-1-yl)acetamide (2ac):**

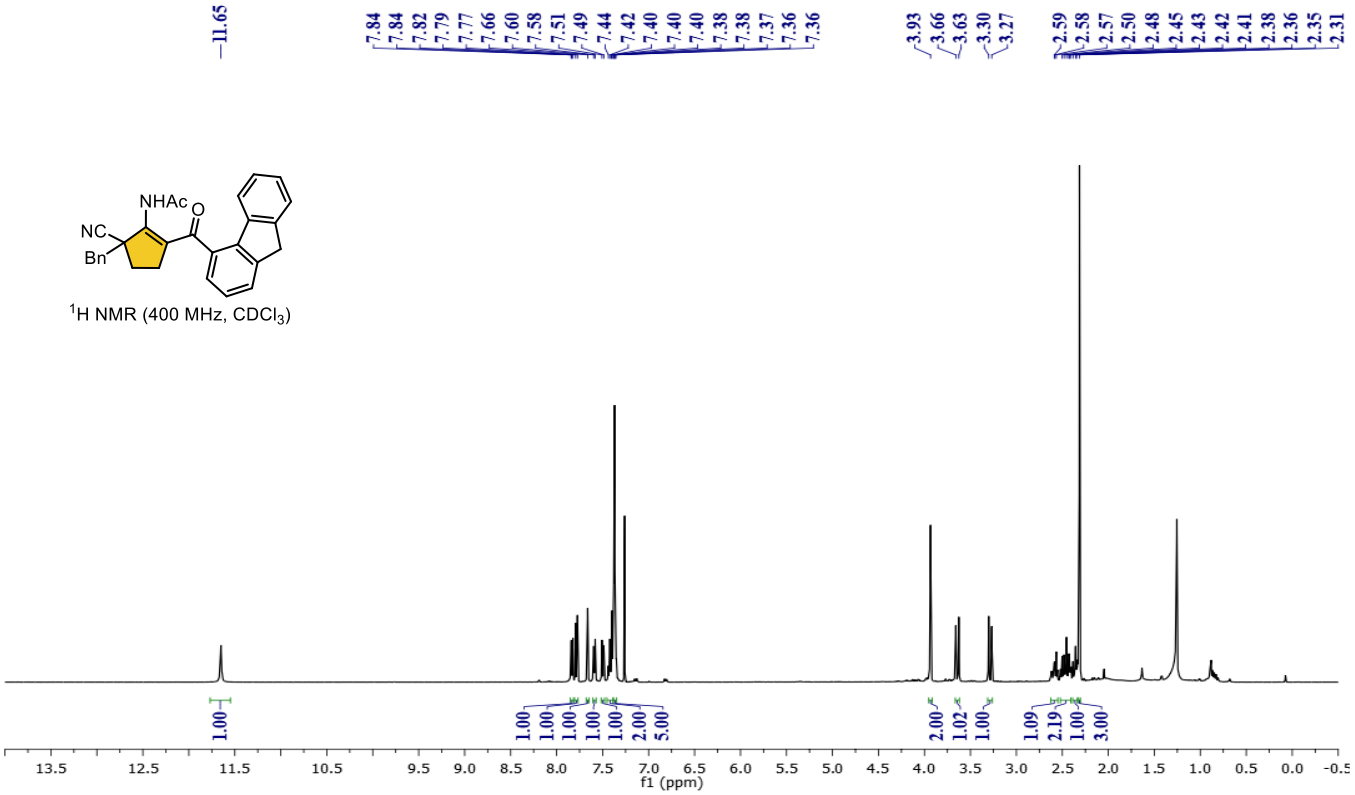


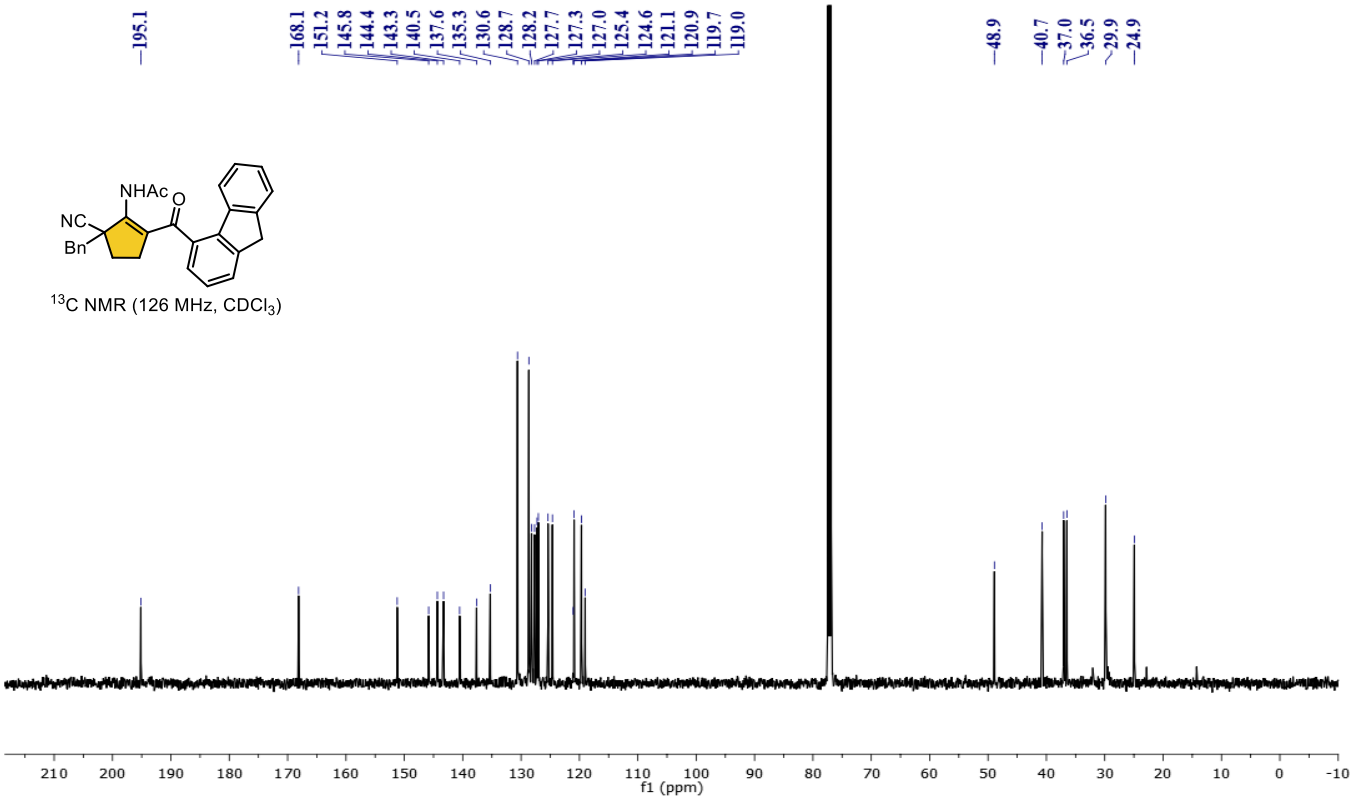
^{1}H NMR (400 MHz, $CDCl_3$)



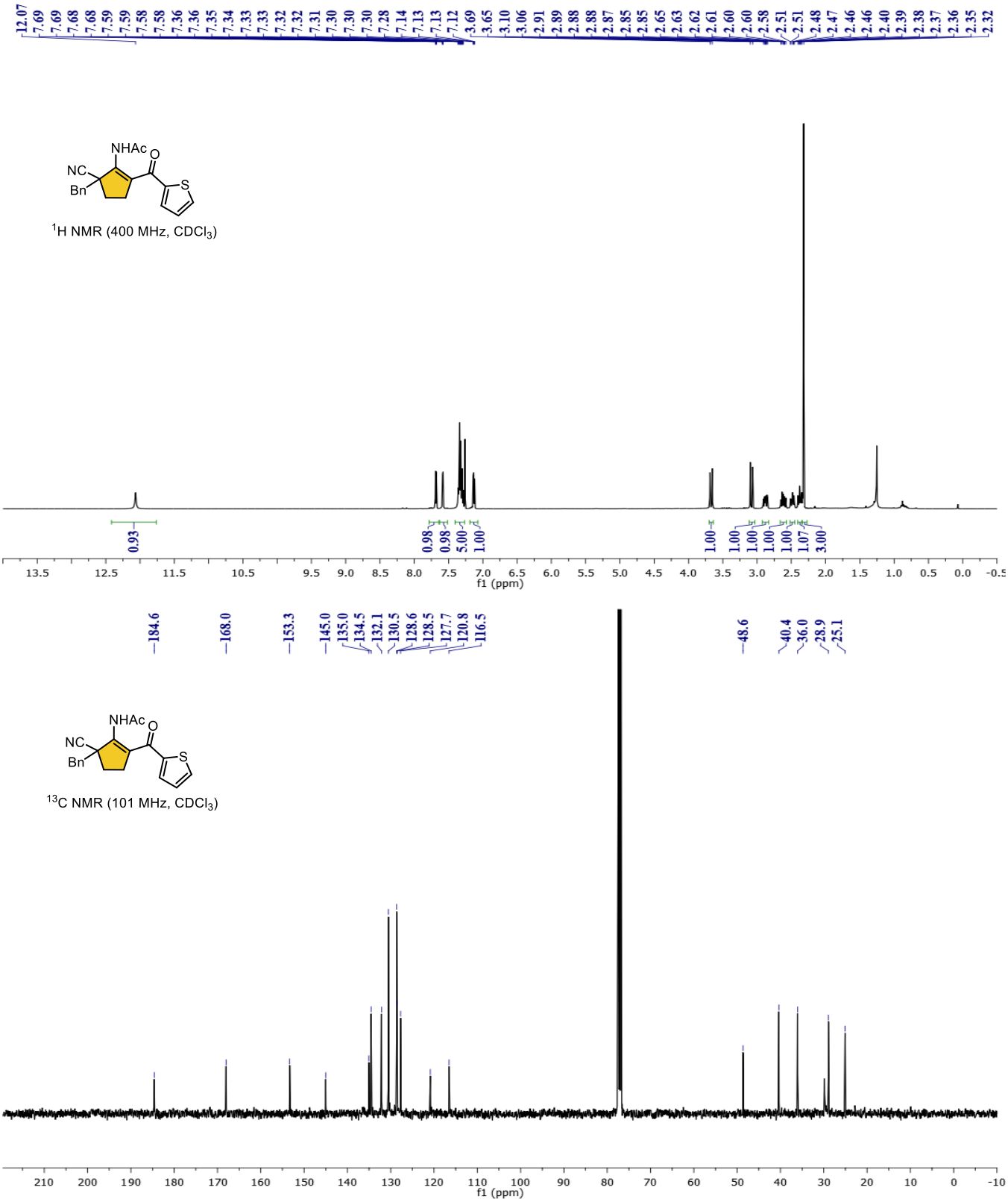
^{13}C NMR (176 MHz, $CDCl_3$)

***N*-(5-Benzyl-5-cyano-2-(9H-fluorene-4-carbonyl)cyclopent-1-en-1-yl)acetamide (2ad):**

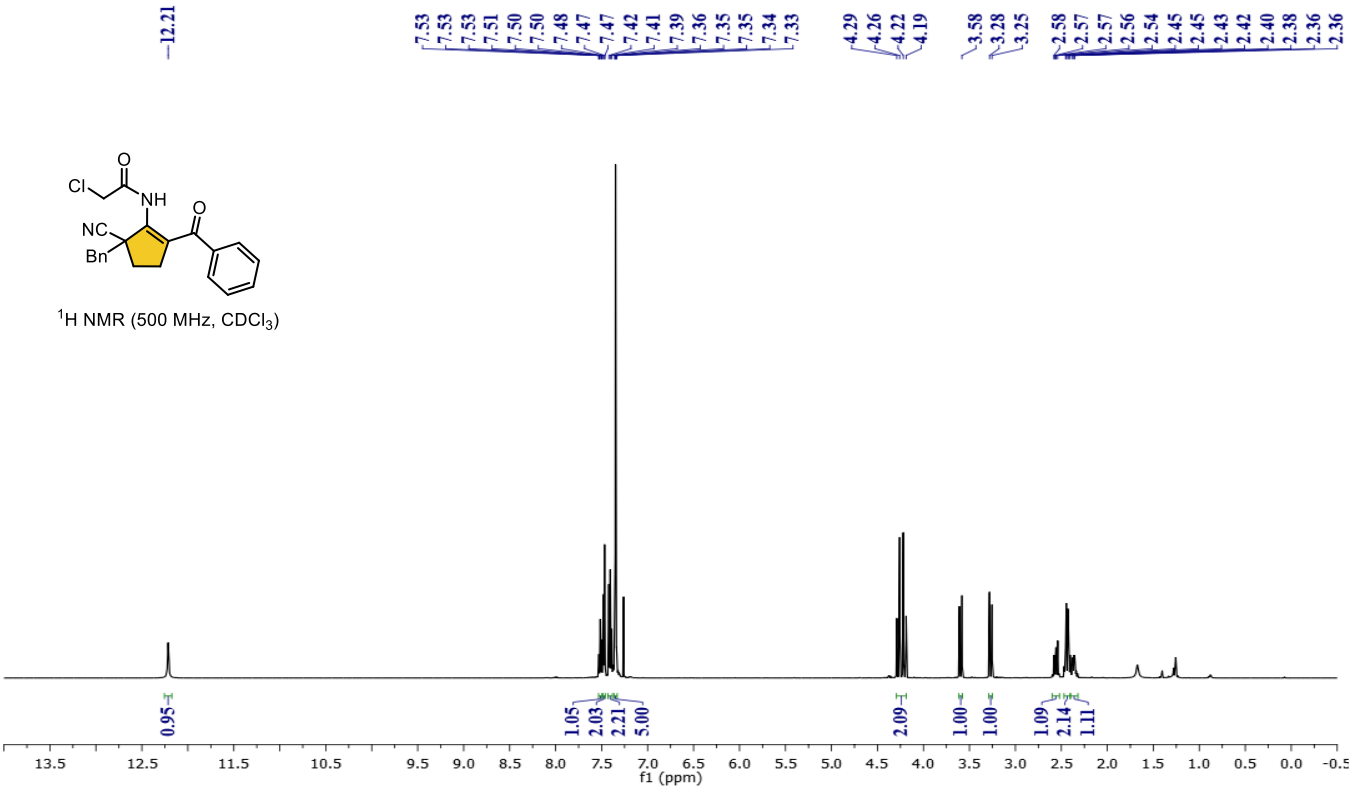




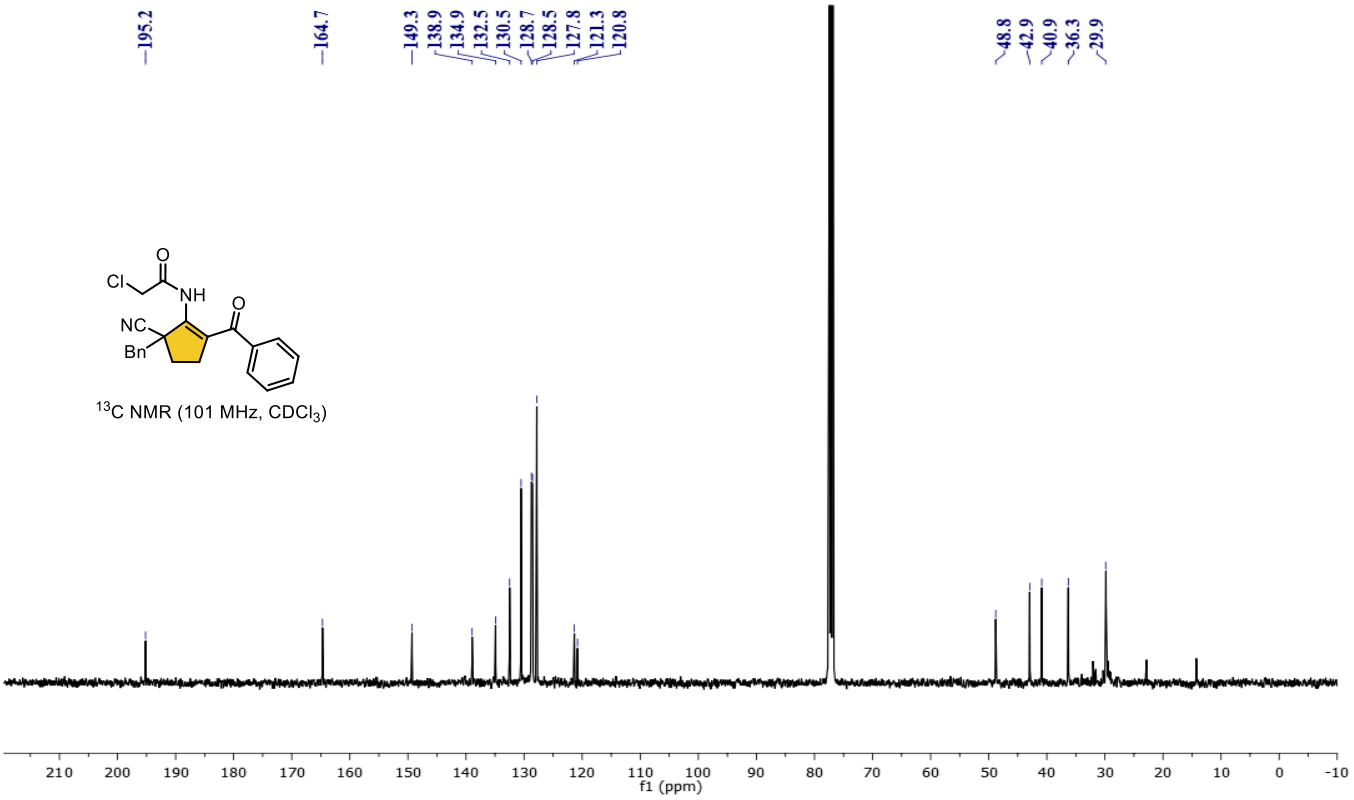
***N*-(5-Benzyl-5-cyano-2-(thiophene-2-carbonyl)cyclopent-1-en-1-yl)acetamide (2ae):**



***N*-(2-Benzoyl-5-benzyl-5-cyanocyclopent-1-en-1-yl)-2-chloroacetamide (2af):**

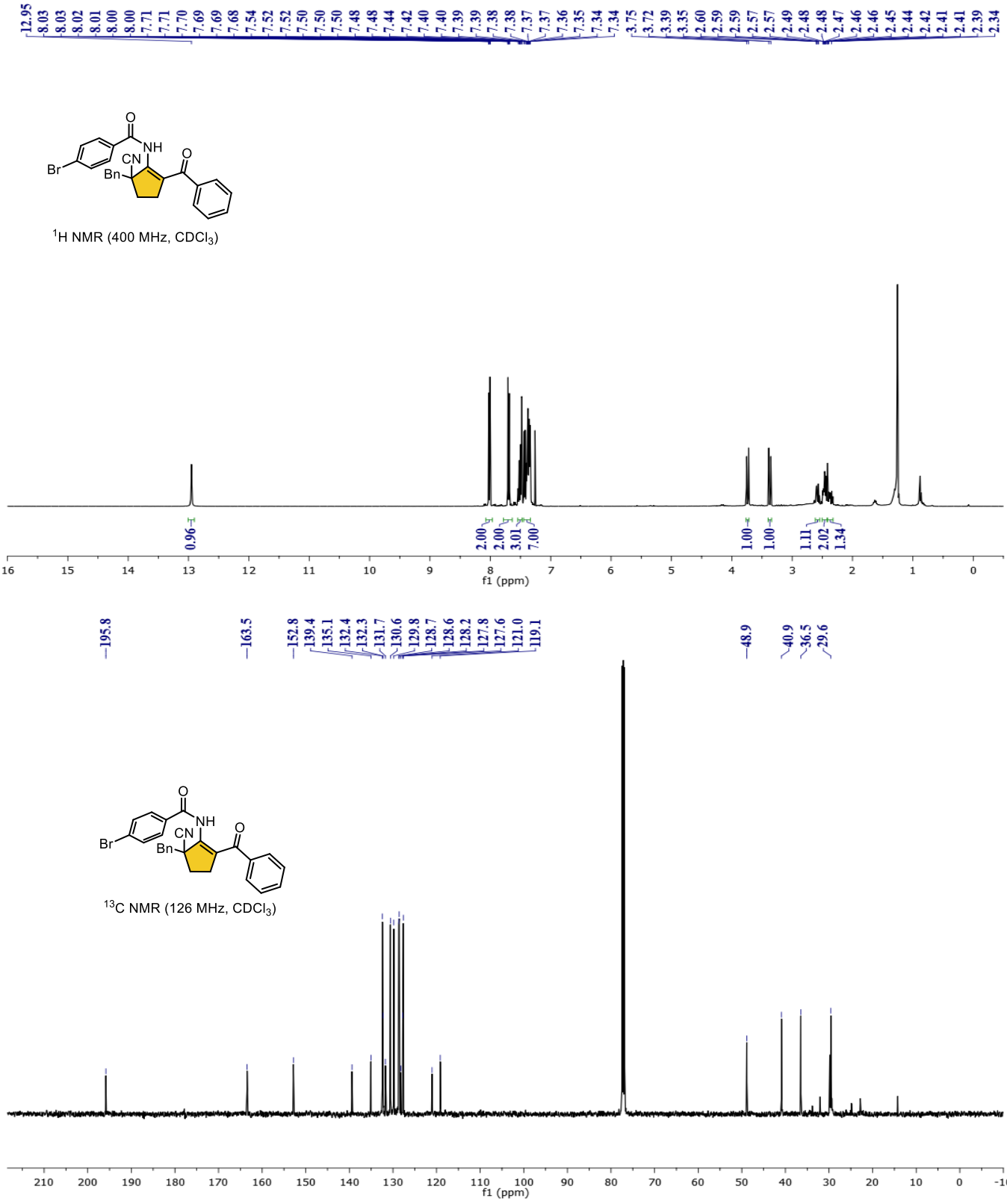


^{1}H NMR (500 MHz, $CDCl_3$)

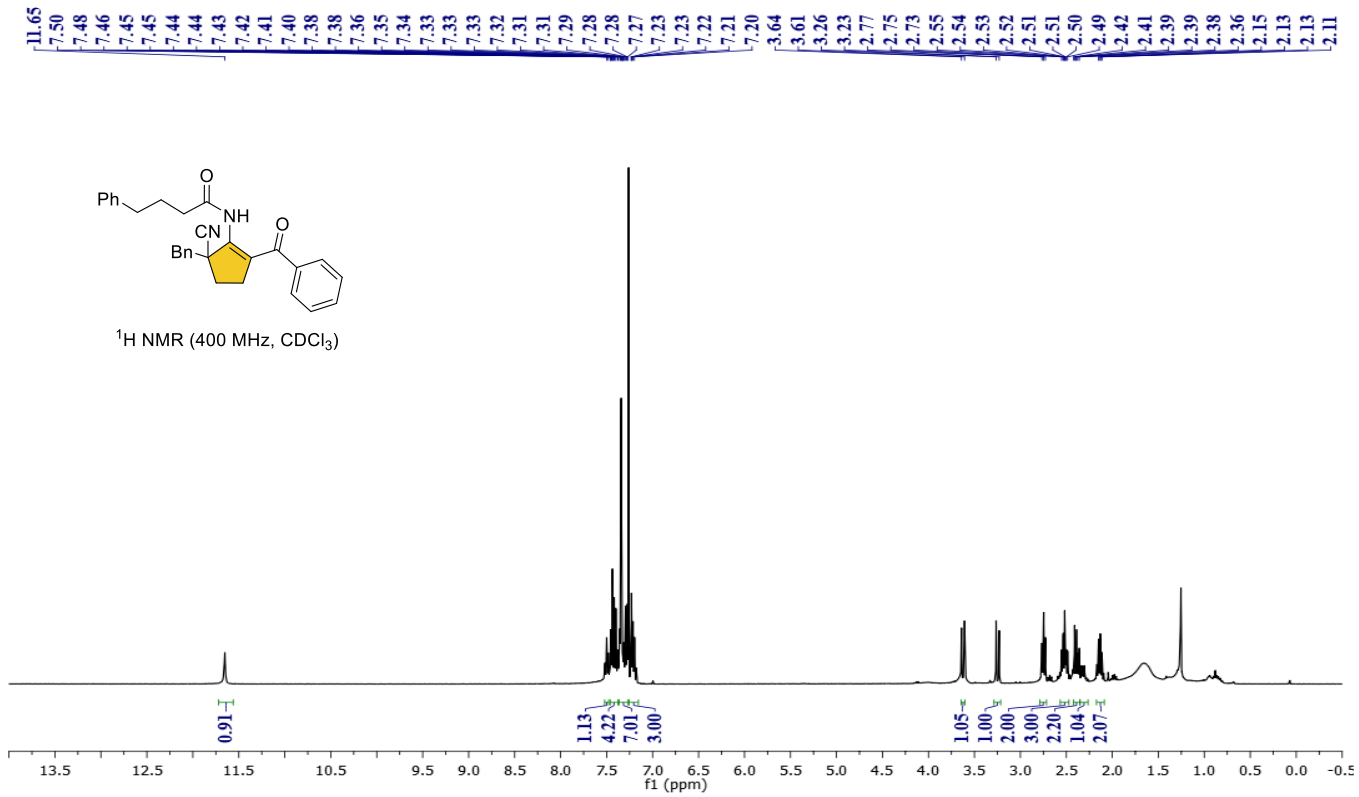


^{13}C NMR (101 MHz, $CDCl_3$)

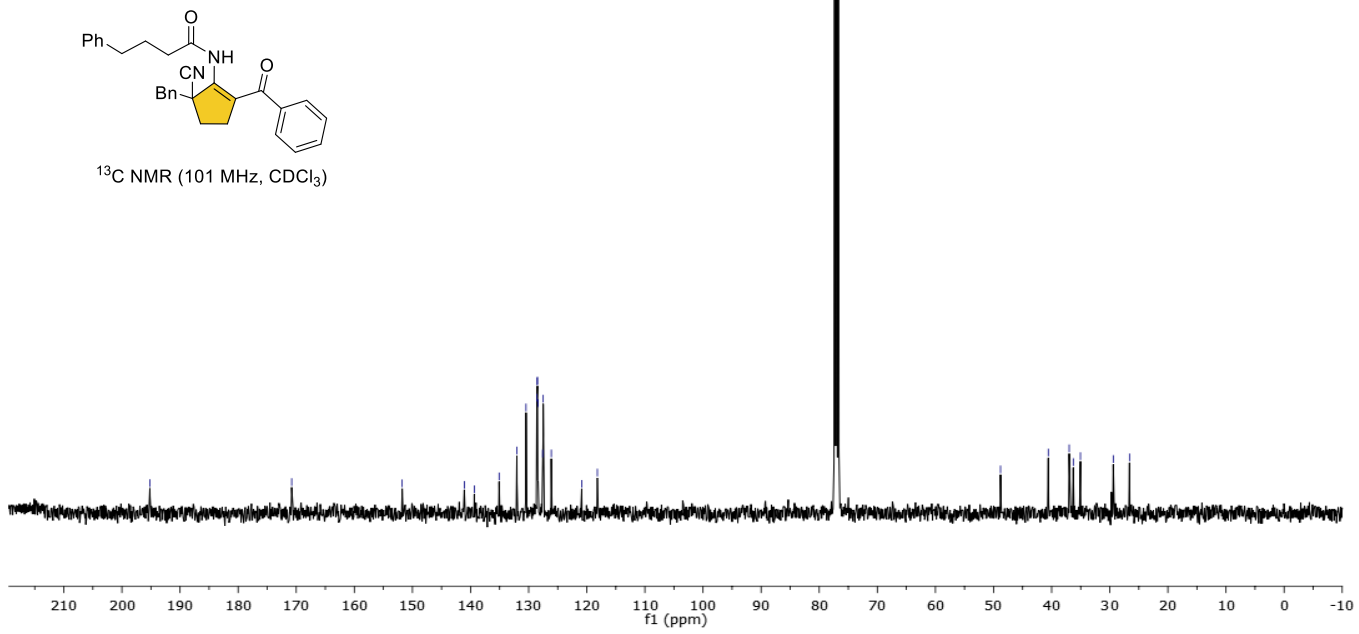
_N_-(2-Benzoyl-5-benzyl-5-cyanocyclopent-1-en-1-yl)-4-bromobenzamide (2ag):



_N_-(2-Benzoyl-5-benzyl-5-cyanocyclopent-1-en-1-yl)-4-phenylbutanamide (2ah):

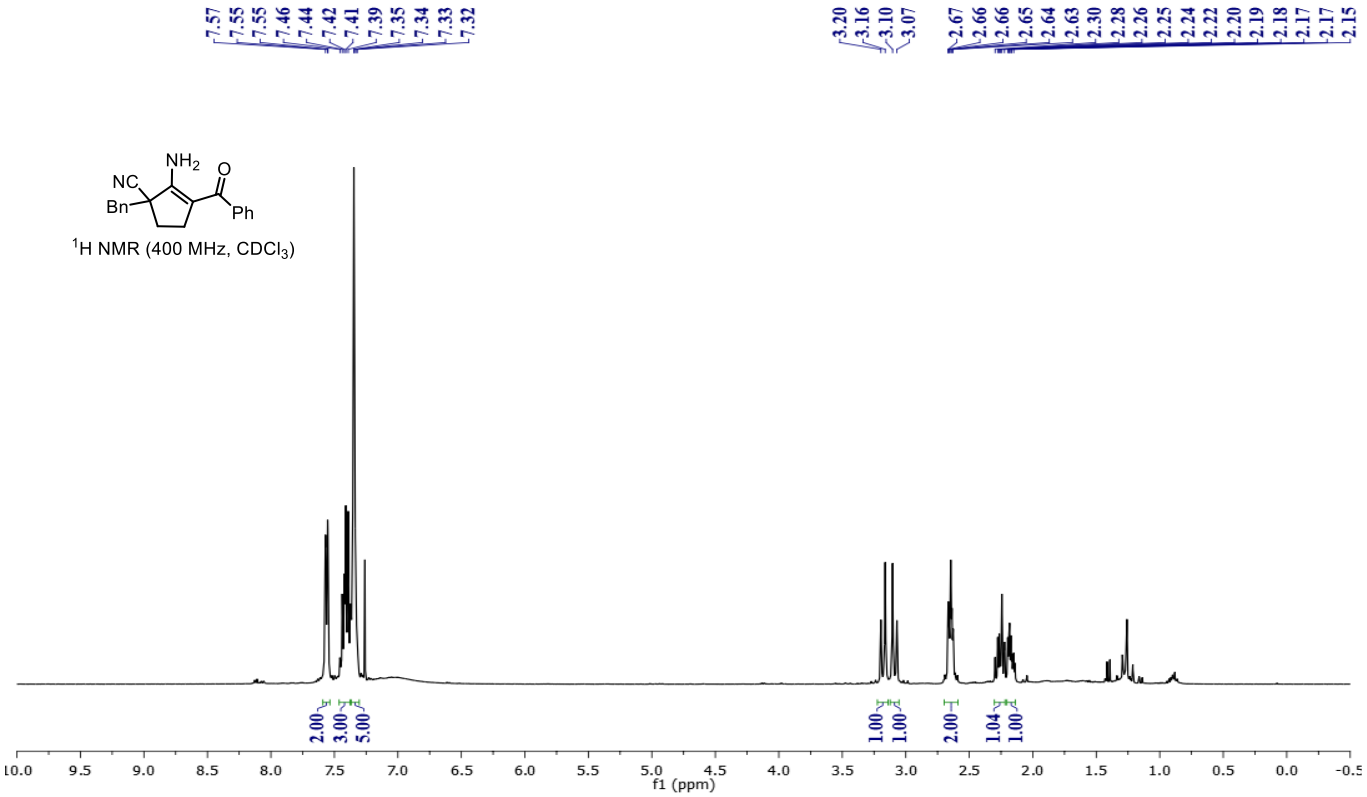


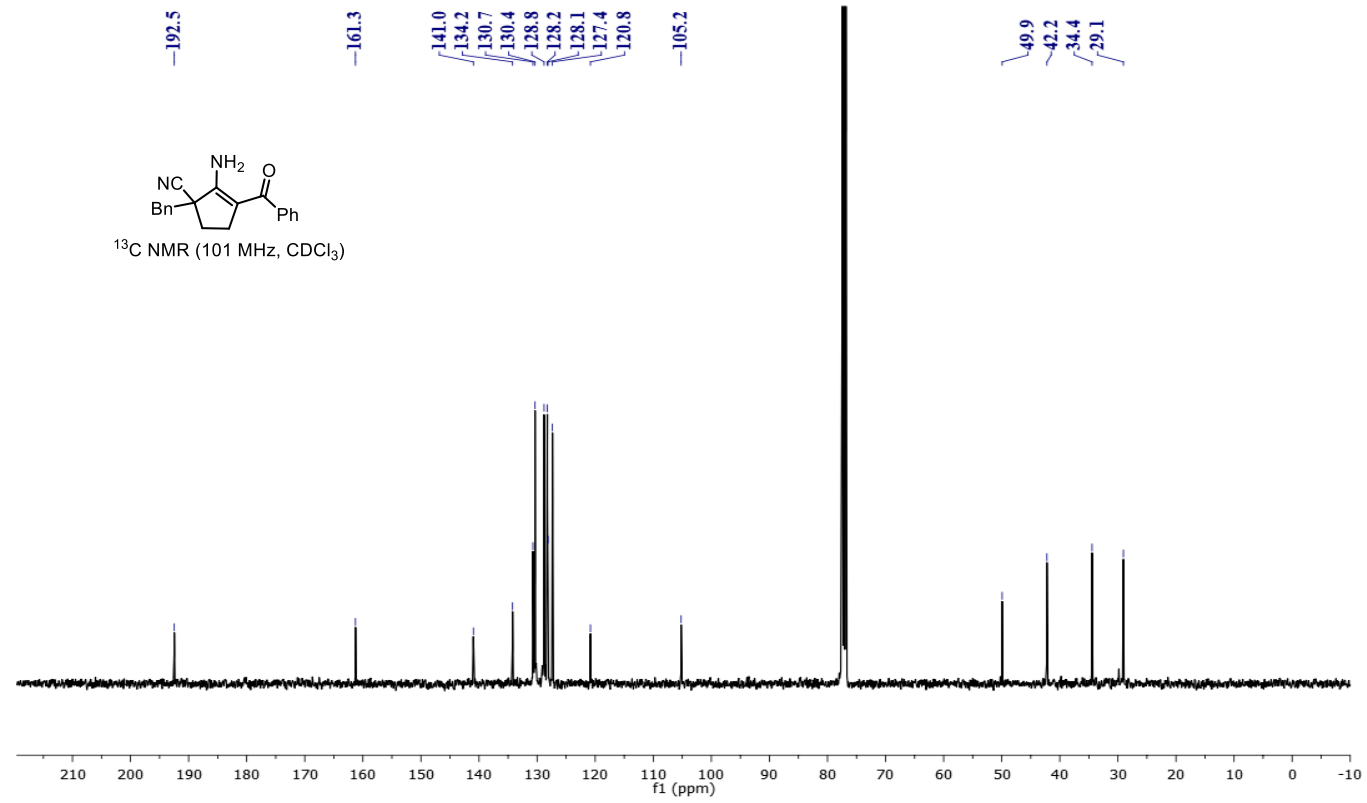
^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (101 MHz, $CDCl_3$)

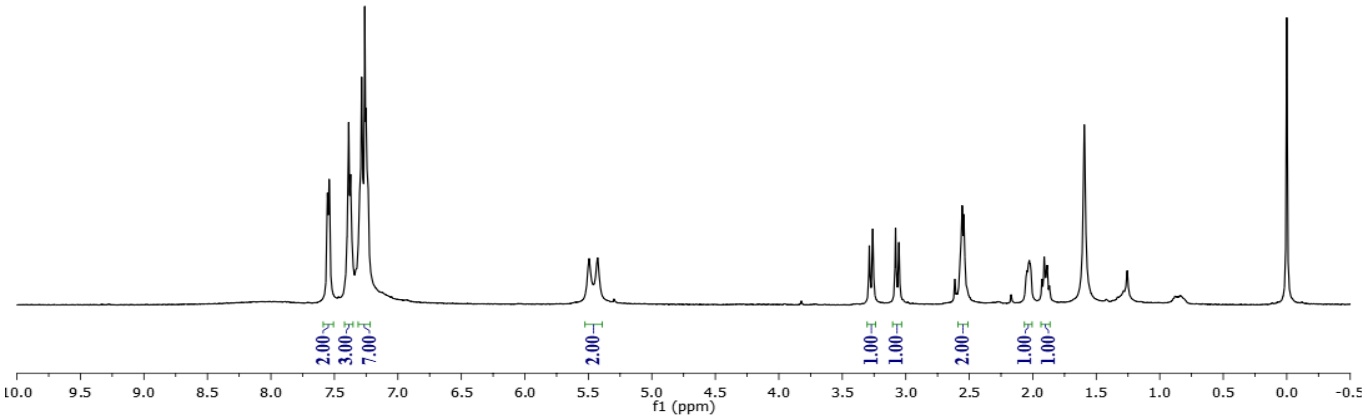
2-Amino-3-benzoyl-1-benzylcyclopent-2-ene-1-carbonitrile (3):

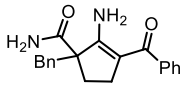




2-Amino-3-benzoyl-1-benzylcyclopent-2-ene-1-carboxamide (4):

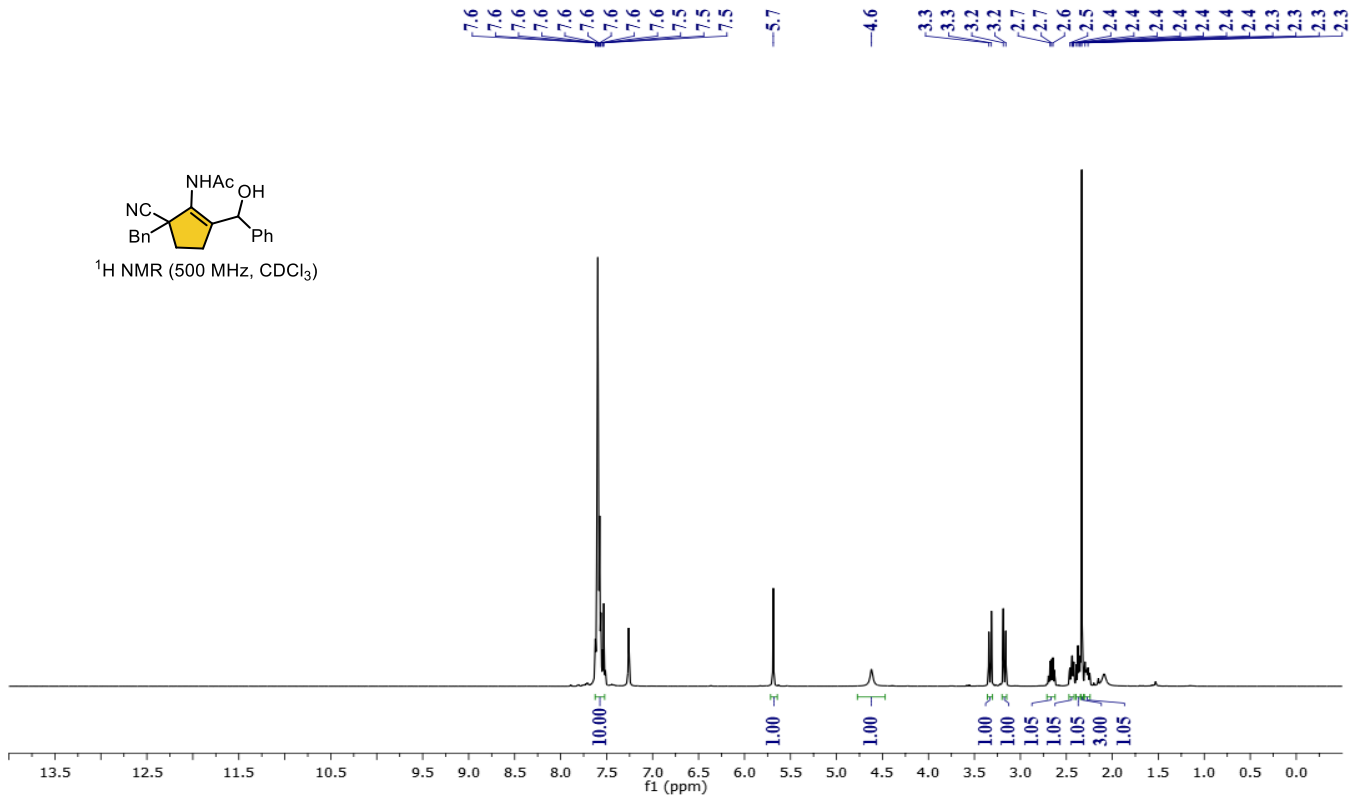
^{1}H NMR (500 MHz, $CDCl_3$)

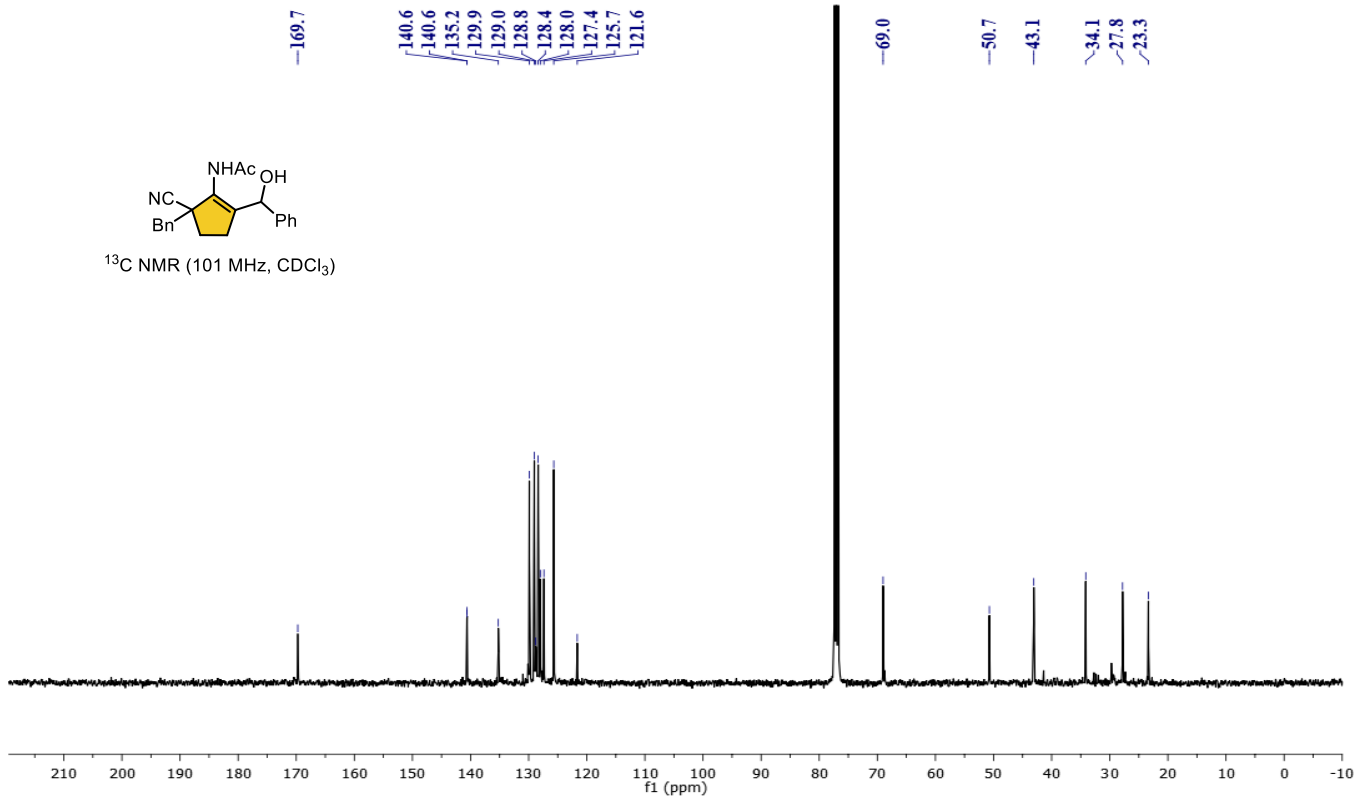




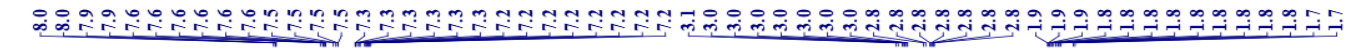
^{13}C NMR (101 MHz, $CDCl_3$)

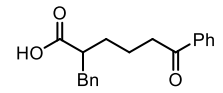
N-(5-Benzyl-5-cyano-2-(hydroxy(phenyl)methyl)cyclopent-1-en-1-yl)acetamide (5):



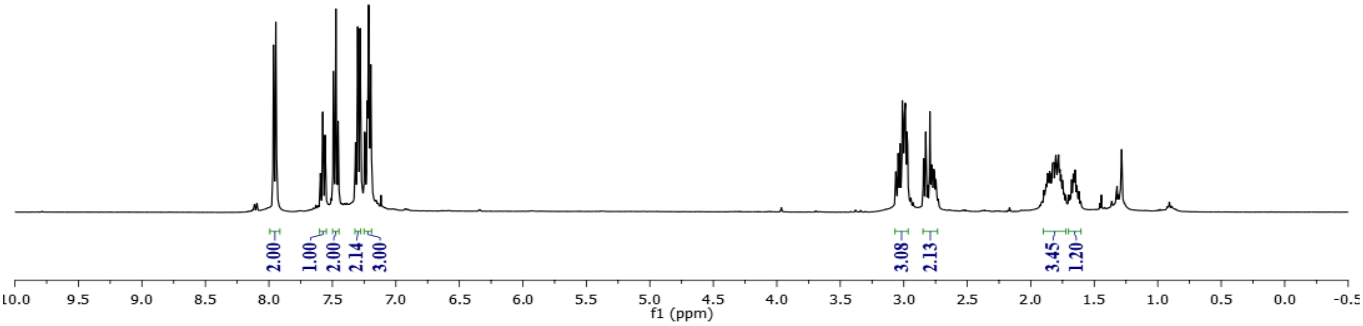


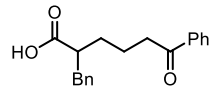
2-Benzyl-6-oxo-6-phenylhexanoic acid (6):





^{1}H NMR (400 MHz, $CDCl_3$)





^{13}C NMR (101 MHz, $CDCl_3$)